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GENETICS

By the same author



The Biological Basis of Human Nature

GENETICS

by

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PREFACE

THIS book is an attempt to present the fundamental features of Genetics: those features of which every educated person should have knowledge. Resemblances and differences among organisms are due largely to diversities in the materials with which the different individuals begin life. This fact forms the guiding principle in the presentation here given. The distinction commonly made between heredity and the mechanism of heredity is therefore abandoned; such a distinction is out of date. Only through knowledge of the materials on which heredity depends, and an understanding of their methods of operation, is it possible to understand the course taken by heredity and variation, so that study of these matters forms the groundwork of genetics.

This groundwork involves detailed facts and relations that must be thoroughly grasped; these are presented so far as possible in sharply defined form; they are in many cases condensed into formal numbered propositions. In the chapters dealing with more general relations, and based on the earlier chapters, the material is presented in the more usual form of continuous discourse. References to sources are collected into notes at the ends of the chapters. For the better known matters, already gathered into books or monographs, reference is made to such collective accounts, from which the original sources can be traced if desired. For more recent knowledge, not yet unified, references are given to original papers; such are more common in the later chapters.

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I

SUBJECT MATTER OF GENETICS

Materials of Heredity and their Operation

Genetics searches for the answer to certain questions concerning organisms. How does it happen that living things differ? How are the differences brought about? How does it happen that some living things resemble certain others, while some are very unlike? What brings about the many degrees and kinds of similarity and difference among living things?

The questions that are dealt with in genetics may be illustrated concretely for man. How does it happen that some are men, some are women? How does it happen that some are tall, some are short; some are stout, some are thin? How is it brought about that some are lighter, some darker in complexion? How does it happen that some have blue eyes, some grey eyes, or brown or black eyes? There are differences of all sorts, great and small, in form of the features, size and shape of the nose, distance apart of the eyes, and in hundreds of other peculiarities of the face and body. What are the causes of these?

Further, some individuals are strong, while others are weak. Some are healthy, some are sickly. Some individuals suffer from tuberculosis, from cancer, or from other diseases, while others are immune. What are the grounds for such diversities? Still more important are differences in 'minds', differences in behaviour. Some persons are feeble-minded, not able to care for themselves or do the ordinary work of life. Others, not actually feeble-minded, are dull. Others are intelligent. Some have great abilities; they are geniuses. Among those that are neither stupid nor geniuses, some are fitted for one kind of work, some for other kinds. There exist similar differences in senses, in tastes, in emotions.

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Genetics deals with all such differences; it inquires as to their source. It deals further with the great differences between organisms, that make men classify them into different species, different genera, families and the like.

Genetics deals also with similarities, for these are merely degrees of difference. It inquires how it happens that some individuals differ little, others much. Twins may be so much alike that they are indistinguishable to the observer. Other children of the same family resemble each other, but less, as a rule, than do twins. Members of the same race are more alike than members of different races. The same sorts of differences and similarities are found in other animals and in plants. They are what give variety and individuality and interest to the world of men and of other organisms, and they give rise to most of the problems and difficulties of the living world. It is the task of genetics to seek for the causes of the similarities and differences among organisms.

There are two main classes of differences between things. On the one hand things may be diverse because they are composed of different materials. An object made of iron is very different from one made of glass, or of lead, or wood, or water, or air. A physician's prescription has tremendously differing effects, depending on the drugs it contains.

On the other hand things may be diverse because they have been treated differently, because of the different conditions under which they exist or have existed. Water under one set of conditions is solid ice, under others it is liquid or vapour. A piece of iron treated in one way—shaped into a certain form—becomes a key that will unlock a door; treated in another way it becomes a knife blade that will cut.

These two classes of differences are shown in a particularly striking way by machines, and also by organisms. An automobile or a typewriter depends in every detail of its structure and its operation on the materials of which it is made. By changing the materials of which the parts of the machine are made, every feature of the machine can be altered. Some materials make good parts, others poor ones. But the structure and running of the machine depend too on the way the

MATERIALS OF HEREDITY: THEIR OPERATION

materials are handled in the factory; depend on the methods used in manufacturing the machine. The same materials can be made into very different machines, by changing the method of manufacture.

Organisms, including human beings, show the same two classes of differences. It has been discovered that in every distinguishable property organisms depend on the materials of which they are composed at the beginning of their lives; that is, on the materials that they receive from their parents. Structure, physiology, mind, behaviour—all may be altered by changing these materials. Different individuals, in man and in other organisms, receive different sets of materials from their parents. And it is found that every feature or quality of the organism—physical, physiological, or mental—can be changed by substituting one kind of material for another. It is found that a great proportion of the differences observed between different persons, or between different animals or plants, are the result of the different materials with which they begin life.

It is the differences that result from these different materials received from the parents at the beginning of life that constitute the special subject matter of Genetics. *Genetics may be defined as an account of the effects of the diversity of materials with which different individuals start life: the effects of the different materials received from their parents.* These effects are commonly classified as heredity, so that Genetics deals largely with heredity. Heredity itself may be defined as the influence on the individuals of the materials which they receive from their parents at the beginning of their lives.

But the structures and qualities and activities of men and other organisms do not depend exclusively on the materials of which they are composed. They depend also—like the structures and qualities and activities of an automobile or other machine—on the way the materials are treated, on the conditions to which they are subjected. The characteristics, the methods of action, can be changed by changing the conditions under which the organism develops and lives. All this is often grouped under the effects of the *environment*; but it

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includes, as different aspects, what in man are called training, education, experience.

In trying to understand men or other organisms, one must always keep in mind these two great classes of influences: heredity, the influence of the different materials with which different individuals begin life; and environment, or the influence of the way these materials are treated, the conditions to which they are subjected. Many of the differences between organisms are due to the former, many to the latter. It is the province of genetics to disentangle so far as possible the action and effects of these two classes of influences. Strictly considered, the province of Genetics is the former: the effects of the different materials of which different individuals are composed. But the two classes of influences are so closely intertwined, their results so fully integrated, that one cannot be dealt with separately from the other.

The Materials of Heredity

How does it happen that different individuals are at the beginning composed of different materials? The different materials of different individuals are received from their parents. The fact that the materials so received differ in different cases is a consequence of certain relations which may be summarized in a preliminary way as follows (details are taken up later):

The parents contain in their cells a large stock of materials of many kinds, with diverse physiological effects; these are in the form of minute particles. Each parent contributes to the child but half of his stock of materials, the other parent contributing the other half. And the half which each parent contributes is taken in a random way, later to be described in full. There is a system of distributing these materials, a system that much resembles the operation of a lottery, so that any child receives a different set of materials from every other.

Just how that lottery turns out for any given individual is perhaps the most important matter of his life. For it is through this system of distribution that each receives his particular

THE MATERIALS OF HEREDITY

endowment, the things on which depend his individuality and his abilities. It is the method by which each receives the capital on which he is to do business for the rest of his life. On the way this distribution of materials from the parents takes place depend more than on any other one thing the individual's personality, powers, fortune and fate. The distribution occurs in accordance with certain rules, and it is these rules that are the foundation of what are called the laws of heredity.

To understand the nature of human beings or other organisms; to understand their likenesses and differences, to understand how later generations are related to earlier ones, the first requisite is to understand these materials and their method of distribution from one generation to the next. Many questions of the greatest interest arise continually, the answers to which depend directly on the way this distribution occurs: What difference does it make what kind of parents one has? Can only inferior or mediocre children come from inferior or mediocre parents? Are the children of superior parents certain to be superior? How important a matter is the stock or family from which one is derived? What can we know beforehand about the children that will be produced by parents of a certain kind? How far can later generations be influenced by selection of the parents in the present generation, and by the way they are mated? What chance is there for the improvement of society, of the race, by selective breeding?

We therefore undertake first a study of these materials and of their distribution from parents of offspring. It will be best to look first at the way in which these materials of heredity were discovered, and at how their method of distribution became known. First a general picture will be presented; later the important matters will be taken up in detail.

Discovery of the Materials of Heredity. General Sketch of their Method of Action

Long ago it was discovered, as everyone knows, that a new individual arises, in most organisms, from the union of two small pieces of material that have been called *cells*—

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specifically, *germ cells*. One of these small pieces of material comes from one parent, one from the other, and the two join to form the beginning of the new individual. The one from the male is commonly called the sperm cell, while the one from the female is called the ovum, or egg. These two minute germ cells unite, giving what we call the fertilized egg. And this fertilized egg is the beginning of the new individual.

In most organisms, as we know, these two minute pieces, the sperm and the egg, form the only connection there is between parents and offspring. This is not true in some of the higher organisms, such as man, but it is true in most organisms. It is therefore clear that in such organisms all relationship between parent and offspring is through these minute bits of material, the germ cells. It is on them that it depends whether the new individual shall be a snail, a fly, a fish, a frog, a bird.

It has since been discovered that the same is true even in animals in which the mother carries the young in her body for a time. This remaining in the body of the mother has very little effect on the nature of the individual produced. It depends on the material of the two minute cells, the sperm and the egg, whether there shall be produced a dog, a horse, or a man. And if a dog is produced, it depends on these whether it shall be a hound, a bulldog, a spaniel, a poodle, or some other variety. In man it depends on these two pieces of material whether the child produced shall belong to the black or yellow or white race. And on them depend in large measure the form, the size, the type of features, and even the physiological and mental characteristics. On them depend the resemblances that the child shows to its parents in all these respects; and on them also depend to a large degree the differences between one individual and another. Practically everything that brings about the relation of parents to offspring therefore lies in these two minute bits of material. They are obviously of extreme importance and interest, so that men set to work, a long time ago, to examine them with microscope and with all other means at their disposal. And in the course of time they found out many extraordinary

DISCOVERY OF THE MATERIALS OF HEREDITY

things about the egg and sperm. The meaning of these things was at first not known. But men made guesses about them, and, as time passed, some of the guesses were verified, so that the significance of many of the things observed has been discovered.

What things are found in the Germ Cells?—The germ cells were early found to contain a complicated miniature apparatus, the *nucleus*. This nucleus was found to contain a number

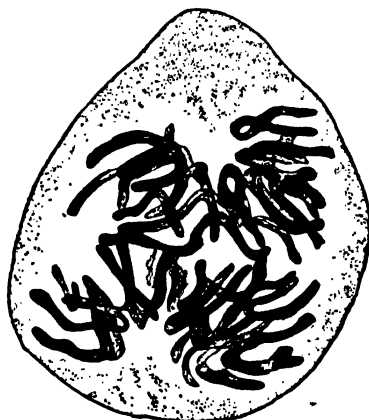


FIG. 1.—*Chromosomes, in the condensed condition, in a dividing cell of the salamander Amblystoma.*

of pieces of machinery, of a curious appearance, which have been called the chromosomes (Fig. 1). These chromosomes are found too in all the cells of the body that is later formed from the germ cells. Although they are continually changing, growing, dividing, operating in various ways, the chromosomes take on at regularly recurring periods in the life of the cell certain clearly marked characteristics. At these most conspicuous periods they appear as rod-like, loop-like or granular structures. When the cell divides, these structures are observed to go through a remarkable and complex series of evolutions (Fig. 2). They arrange themselves about a spindle-shaped structure, and each one splits lengthwise. The two halves then separate, one set of halves moving in one direction, to form a group by itself, while the other halves move

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in the other direction and form another group. Then the cell divides into two, and one group of halves remains in one of the two cells, while the other group of halves remains in the other cell. Then the halves each enlarge to form a complete

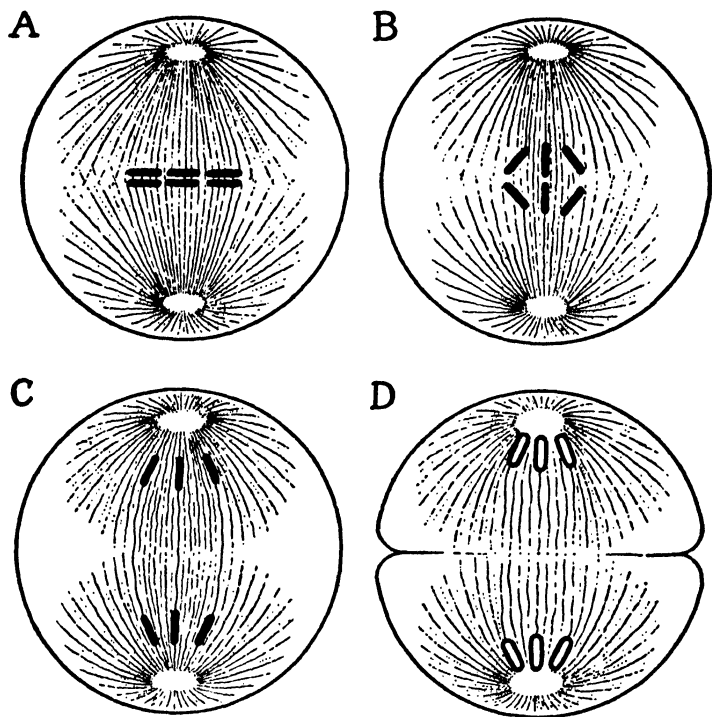


FIG. 2.—Diagram of certain successive stages in the division of the chromosomes and of the cell (mitosis). Only three chromosomes represented. In A the three have split lengthwise; B, C, D show successive stages in the separation of the halves into the two new cells produced.

chromosome; these swell up and become little vesicles, which are pressed together and form a new nucleus for each cell (Fig. 2). And when this new cell comes to divide, these vesicles form by condensation each a new chromosome like the one from which it came; then these chromosomes go through this complicated process of division again.

THINGS FOUND IN THE GERM CELLS

This division of the chromosomes is very precise; each chromosome produces two new ones exactly like itself. Often the different chromosomes in the cell differ greatly in size and form. When each one divides, the two new ones produced are like the particular parent chromosome, in size and in form.

All this appeared marvellous to those who observed it under the microscope, and it still appears so to anyone who follows it in any organism. What does it all mean? What is it that is occurring here?

To pursue the observations further, certain other things that appeared still more remarkable were discovered. In any kind of organism, every one of the millions of cells has a set of these chromosomes. And the number is constant throughout the organism; every cell has the same number. Each kind of creature has its own characteristic number, varying from two in some species to hundreds in others, but for each organism the number is constant. The same number of chromosomes that is found in the cells of either of the parents is later found in the cells of his offspring—with certain modifications that will be mentioned later.

But this fact, that the child has in his cells the same number of chromosomes as either single parent, seemed to the early investigators remarkable. For the sperm is a cell from one parent, the ovum a cell from the other, and the two unite to form the cell that becomes the child. One might expect that when the two united, this would give the child twice as many chromosomes as either of the parents. How does it happen that this is not true? How does it happen that the child has only the same number of chromosomes as each separate parent?

This was long a puzzle. But study with the microscope answered this question. The two parents do not give all of their chromosomes to each germ cell, but only half of them. In forming the germ cells by division of the cells of the parent, a very remarkable thing occurs, a thing that does not occur at any other cell division. In all other cell divisions each chromosome splits into two new ones, so that each new cell gets the same number of chromosomes that the parent cell had (Fig. 2). But in this division to form the germ cells, the

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chromosomes do not split. Instead, half of them go into one of the new cells, half into the other. And so the germ cell, as it is finally formed, has not the usual number of chromosomes, but only half of them. This is true for both the sperm and the ovum.

And so when the sperm and the egg unite, the two produce a new cell that now has, restored, the usual number of chromosomes. The sperm cell and the egg cell are really only half-cells, so far as their chromosomes are concerned; their union produces a complete cell again, and this now develops into a new individual—every one of his cells containing the full number of chromosomes—half from his father, half from his mother.

What is the function of the Chromosomes?—Imagine an investigator who, working with infinite pains and taking a very long time, discovers all these strange facts. Naturally, he is stirred, he is excited. He asks himself, what can these things be? What is their function? What do they accomplish by all these complex evolutions, by splitting themselves accurately into two pieces to form new chromosomes, by reducing their number to half, when a new individual is to be formed, and by restoring the usual number by union of two pieces? This must all mean something. What does it mean?

In trying to answer that question, the investigators reflected on certain facts. First, these chromosomes are found in the eggs and the sperm, which unite to form a new individual, a new person. Second, these germ cells are the only connection that exists between parent and offspring; they are all there is that comes from the parents. Yet the child produced from their union is in many details like the parents. This likeness *must* be brought about by the minute germ cells that unite to form the fertilized egg. Such likeness to parents may show itself in respect to a very great number of different characteristics—in respect to form of the different features, colours, size, physiological peculiarities, and the like. This seems to require that this minute bit of material, the fertilized egg, should be very complex. And very complex it is found to be, in the matter of these chromosomes.

FUNCTION OF THE CHROMOSOMES

Are the Chromosomes the 'Material of Heredity'?—And so the idea came to investigators that perhaps this complex apparatus of chromosomes is what brings about the likeness of children to parents. This likeness of parent and offspring is one of the manifestations of heredity; it was formerly considered that heredity consisted only in such likeness. So the early investigators said: Perhaps the chromosomes are the 'materials of heredity'. This would account for the exactness of their behaviour, the precision with which they divide, and the accuracy of their distribution in the body.

But how can it be discovered whether this interesting idea is a true one? How can it be determined whether it is indeed this apparatus of chromosomes that brings about likeness to parents, that brings about heredity?

Proposed Tests.—The only chance for doing that is to find out whether changing the chromosomes of the fertilized egg changes the hereditary characters of the individual. Suppose that, after the sperm and egg have united in fertilization, one could reach in with a hook and pull out one of the chromosomes; would that make any difference in the nature and characteristics of the individual that develops from that egg?

It has not been possible to perform this experiment in just that way, but it has been possible to do what amounts to the same thing. It has been possible to answer the question: What difference does it make to the new individual if one of his chromosomes is removed from the original cell that produces him? The answer to that question will be taken up in a moment. But before this is done, another experiment must be proposed.

It is of great interest to find out what difference it would make if one of the chromosomes could be taken out. But still more interesting would be the answer to the question: What difference would it make if we could substitute one chromosome for another? What difference would it make if we could hook out one of the chromosomes, and put another one, taken from another cell, in place of it?

That question, too, it has been possible to answer. The method of work has not been so crude as that of putting in a

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hook and pulling out one chromosome, then poking another into its place. But it has accomplished essentially the same thing.

Results of removing a Chromosome, and of substituting one Chromosome for another.—These two questions must be kept in mind: (1) What difference does it make if one of the chromo-

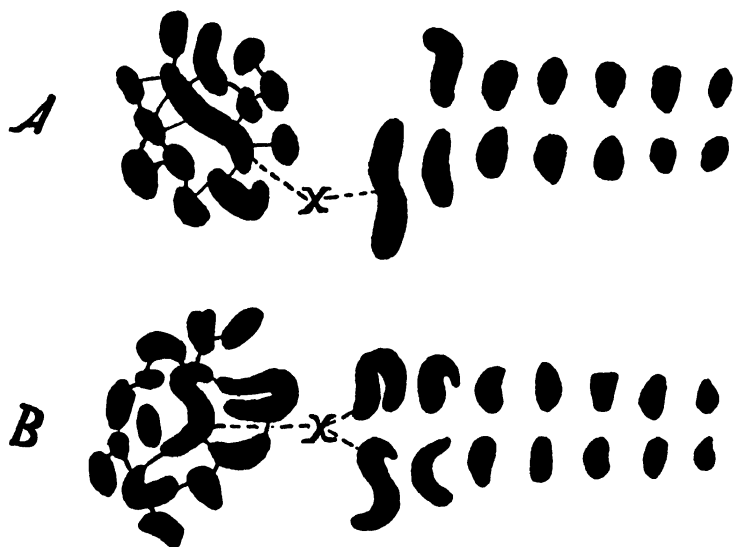


FIG. 3.—The male (A) and female (B) groups of chromosomes in a bug, *Protenor*, after Wilson. At the left in each case is shown the group of chromosomes as it appears under the microscope. At the right are shown the pairs of chromosomes constituting the group, arranged in order of size. X, the X-chromosomes.

somes is removed from the original cell that forms a new individual? and (2) What difference does it make if we substitute one chromosome for another?

The answers to these questions were found in what happens in nature itself. It was found that, in the ordinary production of offspring, one of the chromosomes is omitted from some of the cells, though it enters the others. And it was found that this does, indeed, make a very great difference in the nature and characteristics of the offspring produced.

RESULTS OF REMOVING A CHROMOSOME

Concretely, it was found that in the males of many organisms the number of chromosomes in the cells is odd, while in the females of those same organisms, the number is even (Fig. 3). The females have one more chromosome than the males in every cell. The set of chromosomes in the cells of the males is exactly like the set in the females, save that one of those present in the females is lacking in the cells of the males.

This has remarkable results in the production of the germ cells from which new individuals are to develop. In producing these germ cells, the original cells from which they come divide each into two germ cells (Fig. 4), half the chromosomes going into one of the new cells, half into the other. In the female (B), since the number of chromosomes is even, all of the cells get the same number of chromosomes. If the number in the mother is fourteen, the number in each germ cell from the mother is seven.

But in the male (A), since the number of chromosomes is odd, the results are different. At the division in which the chromosomes are distributed to the germ cells, half of the germ cells receive one more chromosome than the other half. In half of the sperms, one chromosome is omitted, while it is present in the rest of the sperms.

This presents an opportunity to determine what difference it makes if one chromosome is omitted. The egg cells (ova) are all alike in the number of their chromosomes. Half of them unite with sperms that have the full set of chromosomes, half unite with the sperms that have one chromosome omitted (Fig. 5). That is, there is one set of fertilized eggs with a full set of chromosomes, another set with one chromosome lacking. Both kinds develop into individuals. What difference does the omission of one chromosome make?

Differences between the Sexes.—It makes a tremendous difference. It makes a difference to practically every characteristic of the individual. It brings about all the differences, physical, physiological, temperamental, mental, that distinguish the male and the female. It brings about many of these differences rather directly, many others indirectly, through a long chain of processes, but in the end all the characteristic

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differences between the male and the female go back to this difference of one chromosome in the cells that produce them.

For we find that the eggs that contain the full set of chromo-

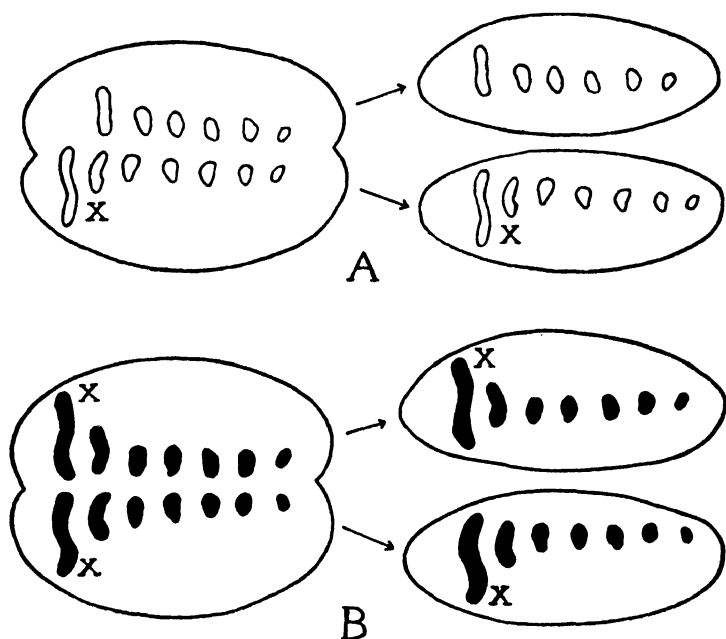


FIG. 4.—This and Fig. 5 are diagrams to illustrate the chromosome combinations in the formation of germ cells, in males and females. The chromosomes of *Protenor* (Fig. 3) are employed as the basis of the diagram. The chromosomes of the male are represented in outline, at A; the chromosomes of the female in solid black, at B. At the left is represented in each case a cell of the parent individual—in the male with six pairs of autosomes and one X; in the female with six pairs of autosomes and two X's. At the right are the germ cells. Half of the germ cells from the male have an X, half do not; while all the germ cells from the female have an X (see Fig. 5 for continuation of the diagram).

somes develop into females, the eggs that lack one of the chromosomes develop into males. And it has been fully proved, by a great variety of observations and experiments, that the difference of sex is certainly due to the original

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chromosome difference. The same egg that would produce a female, actually produces a male if one of the chromosomes is lost or is lacking. Some of the observations and experiments that prove this to be true will be dealt with in later sections.

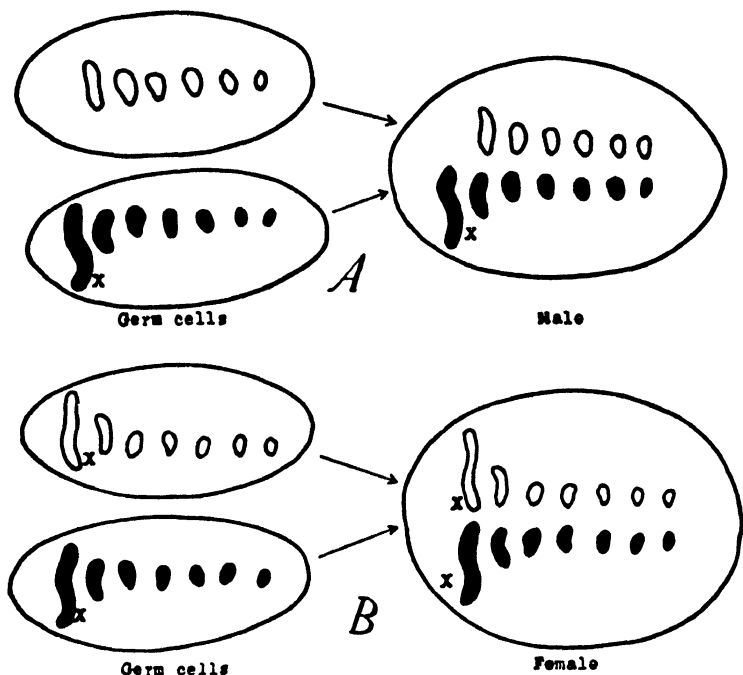


FIG. 5.—Continuation of the diagram of Fig. 4. Formation of male and female individuals (fertilized eggs) by the union of germ cells from the male and female parents. Chromosomes from males represented in outline, from females solid. A, formation of a male individual by union of a male germ cell bearing no X with a female germ cell that bears an X. B, formation of a female individual by union of a male germ cell bearing X with a female germ cell likewise bearing X. The X-chromosome of the male parent thus goes only to his daughters, not to his sons.

This discovery about sex and its relation to chromosomes was the first great step in finding out certainly what is the material on which heredity depends, and it made possible all the others. To that extent the question is answered: What difference does it make if one chromosome is removed from

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the egg cell? The answer is that it changes a female into a male. It brings about all the differences that there are between the two sexes. This proves that the chromosomes are indeed materials of heredity, in the sense that changing them alters the characteristics of the individual.

This was a very great discovery. And it was still greater because it opened the way to answering other questions. In particular, it opened the way to answering the second question: What difference will it make if one chromosome be substituted for another? For it gave, as will be seen later, a method of tracing a particular single chromosome—one derived from the father—through a long series of generations, knowing in which of the descendants it is present, and in which it is replaced by some other chromosome. And so it can be determined whether that particular chromosome has effects that others do not have.

This is what led to the unravelling of the whole tissue of heredity, in its relation to the materials passed from parents to offspring. The facts and relations must therefore be examined carefully. But before this is done, certain further facts about the relation of sex to chromosomes must be considered. These are of great interest in themselves, and they must be known if one is to understand how the further facts of heredity were discovered.

As just set forth, in some organisms the differences between males and females are due to the fact that the male lacks one chromosome that is present in the female. This chromosome that is present in the female, but is lacking in the male, is known as the X-chromosome. In many species, the X-chromosome differs in size or form from the other chromosomes.

But in many species, the male, instead of lacking the X-chromosome entirely, has in place of it a small chromosome, which is almost without function (Fig. 6). This small one, present in the male, but not in the female, is commonly called the Y-chromosome. In man the male has such a small Y-chromosome, while the female has in place of it a larger X-chromosome (Fig. 19).

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In still other species, the special chromosome that the male has—the Y-chromosome—is not smaller than the X of the female, but is of a different shape. This is the case, for example, in the fruit-fly (*Drosophila melanogaster*), which has been studied in respect to these matters more thoroughly than any

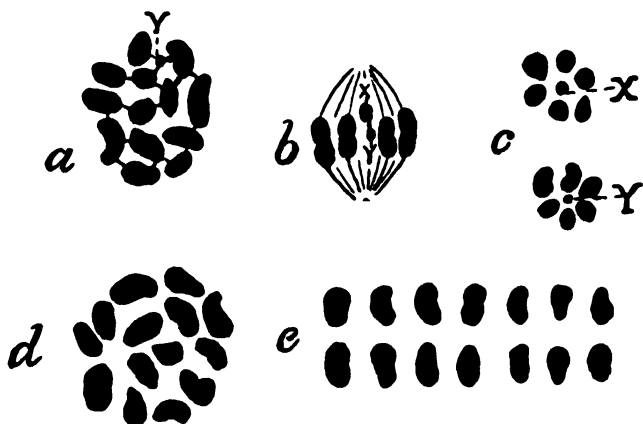


FIG. 6.—Male and female groups of chromosomes in an animal (*Lygaeus*) in which the male has a small X-chromosome, after Wilson. a, The male group of fourteen chromosomes as seen under the microscope. b, The process of division of this group into two groups of seven chromosomes each, in the formation of germ cells. c, The two groups of seven chromosomes each in the two kinds of male germ cells formed, one containing the chromosome X, the other the smaller chromosome Y. d, The female group of fourteen chromosomes, as seen under the microscope. e, The seven pairs constituting the female group, in order of size.

other organism. In this animal the Y-chromosome is hook-shaped, while the corresponding X-chromosome of the female is straight (see Fig. 7). In such cases physiological study shows (as will later appear) that the Y-chromosome is almost without function.

There is thus a series of gradations among different species. The males have one chromosome that, in different cases, is inactive, small, or entirely lacking, taking the place of a fully developed functional chromosome (X) that is present in the

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female. The loss of the activity of this chromosome in some way causes the egg to develop into a male instead of a female. What the nature of this physiological action is that causes the difference of sexes will be discussed later.

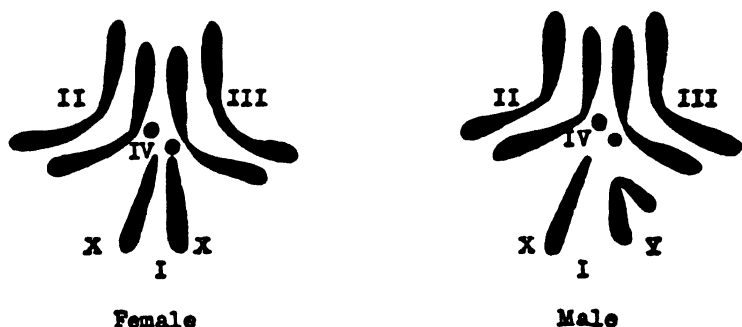


FIG. 7.—The two groups of chromosomes in the fruit-fly, *Drosophila melanogaster*. The female group at the left, with two straight X-chromosomes. The male group at the right, with one straight X and one bent Y. After Morgan, Bridges and Sturtevant, *The Genetics of Drosophila*. The Roman numerals I to IV are the designations commonly employed for the different pairs, the two X's (or X and Y) constituting pair I.

Relation of Chromosomes of Parents to those of Offspring.—Certain general relations of chromosomes in parent and offspring must be held clearly in mind, if one is to understand the further relations of chromosomes to heredity. It will be well to arrange these in a series of propositions:

1. Every individual gets the chromosomes of its cells half from its mother, half from its father (or in some cases one less than half from its father).
2. The chromosomes that it gets from one parent are like those that it gets from the other parent, except that from one parent it may get a large X-chromosome, while from the other it may get a small Y-chromosome (or none).
3. In many organisms, the different chromosomes of the cell are of diverse types, unlike in size and form. Some are round, some are straight, some are V-shaped. This is true in the fruit-fly, for example (Fig. 7).

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4. One of each type from the mother goes into the fertilized egg; also one from each type passes from the father into the fertilized egg.

5. So the chromosomes of the fertilized egg, and of the individual that it forms, are in pairs, one chromosome of each pair from the father, one from the mother (Fig. 5).

6. In some organisms, as in the fruit-fly, the two members of a pair remain side by side, throughout life, so that we find the chromosomes always in pairs. We know that one member of each such pair came originally from the father, the other from the mother.

7. In the female, the two members of each pair are alike. The one that comes from the mother is exactly similar to the one that came from the father; and this is true for all the pairs.

8. But the male has one pair in which one of the chromosomes is smaller or of a different form, or is lacking entirely. This is the chromosome that we have called *Y*; it comes from the father only.

9. In place of this unequal pair the female has a corresponding equal pair of large chromosomes. The large one that corresponds to the *Y* of the male we have called *X*. But, since the other one of this pair is just like it, we must call it *X* too. That is, the female has a pair of *X*-chromosomes.

10. The corresponding pair in the male has only one of these large chromosomes that we call *X*, with or without another of different form that we call *Y*.

11. Thus the correct way to express the difference between the sexes is that the female has two *X*-chromosomes, while the male has but one *X*-chromosome (accompanied in some species by a *Y*-chromosome).

Substitution of one Chromosome for another.—Keeping the above facts in mind, we can discover the answer to the second question proposed above. That question was: What difference does it make if we substitute one chromosome for another? We discover that it may make a great difference. We discover that by different substitutions of chromosomes we can change the organisms in a great many ways. We discover that different *X*-chromosomes have very different effects on

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development. That is, different X-chromosomes are physiologically diverse in their action, producing individuals with different characteristics.

This discovery is made possible by the following facts, which must be thoroughly fixed in mind—(see Figs. 4 and 5):

1. The mother gives one of her two X-chromosomes to each child.
2. The father gives his X-chromosome to half his offspring, his Y-chromosome to the other half.
3. The offspring that get the father's X-chromosome become females (since they have also an X-chromosome from the mother).
4. The offspring that get the father's Y-chromosome become males. They get their single X-chromosome from their mother.
5. Hence, the father's X-chromosome always passes to his daughters, never to his sons.
6. The sons get their one X-chromosome exclusively from the mother.
7. Daughters get one X-chromosome from the mother, one from the father.

We know therefore that in the next generation the father's X-chromosome will be found in his daughters, not in his sons. So if the father's X-chromosome produces some distinctive effect, this effect will be seen in his daughters, not in his sons. And since the rules given above hold also in later generations, the father's X (as distinguished from the mother's) may be traced for generation after generation, and its distinctive effects observed. In the children or grandchildren an X from the father can be substituted in place of one from the mother.

An example will show how this works; it will be taken from the fruit-fly, *Drosophila* (Fig. 8), in which these matters have been studied most thoroughly.¹ This is the small insect often seen flying about bananas or other fruits. It is in many respects the classic organism for genetics.

In the fruit-fly the compound eye usually has a great number of units or facets, gathered into an oval shape (Fig. 9). But sometimes there are individuals in which the eye is abnormal. In such cases many of its outer facets are incom-

SUBSTITUTION OF ONE CHROMOSOME FOR ANOTHER

pletely developed, so that there is merely a broad bar of complete facets across the eye (see the Fig.); this is spoken of as 'bar-eye'. For the experiment a mother is selected that has the full number of normal facets, while the father has the bar-eye. In Fig. 9 are shown the head and eyes of the two parents.

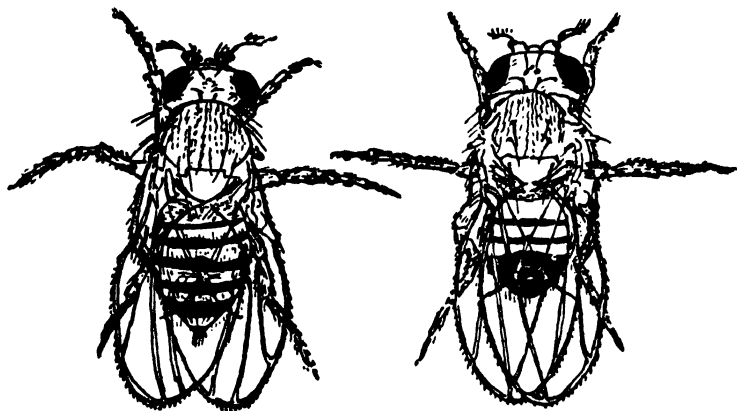


FIG. 8.—*The fruit-fly or banana-fly, Drosophila melanogaster, on the study of which much of our knowledge of heredity is based. Female at the left, male at the right. After Morgan, Bridges and Sturtevant, The Genetics of Drosophila.*

The figure shows also the X-chromosomes of the two parents. The mother's two X's are shown in black, while the father's single X is shown in white; this makes it possible to follow the father's X in the later generations.

We know that in the next generation the sons have no X from the father, while all the daughters contain one from the father (as well as one from the mother). And it is found that the daughters have the bar-eyes, like those of the father, while the sons have not (Fig. 9).

Thus all the children that get an X-chromosome from the father have eyes like the father, while the rest do not. As there may be 200 offspring in a family of the fruit-fly, this result is very striking. A hundred daughters, having their father's X, have also their father's eyes; a hundred sons, lacking their father's X, lack also his type of eyes.

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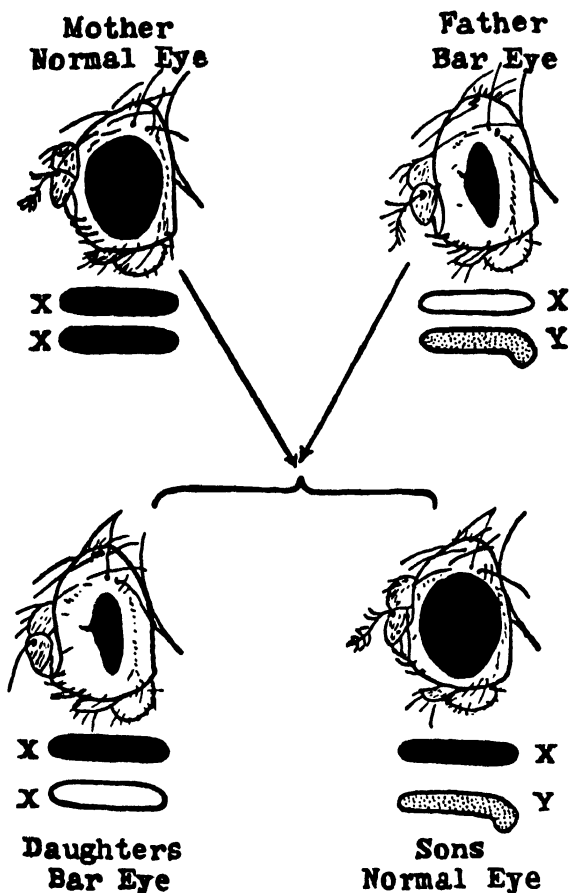


FIG. 9.—Bar-eye and normal eye in *Drosophila*, and their method of inheritance when a mother with normal eye is mated to a father with bar-eyes. The dark area in each eye represents the region occupied by the normal facets of the eye; in the bar-eyed individual this is reduced to a narrow bar. Below each figure of the eyes are shown the X-chromosomes of the individual, those from the mother (normal) being shown in black, those from the father in white. All individuals that have an X from the father (white) have the bar-eye. In consequence the daughters are like the father, the sons like the mother.

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The bar-eyes have thus gone along with the father's X. One is led therefore to suspect that the father's X-chromosome may be abnormal, and that this is what produces the abnormal eyes. If this is the case, then in later generations any individual that gets an X-chromosome descended from that of the father will have bar-eyes.

Is this true? It may be tested further, as follows: The daughters produced in the experiment just described have one X-chromosome from the original father (white), one from the original mother (black). Mate these to their brothers, that have only an X-chromosome from the mother (black).

Fig. 10 shows the result. These daughters give X-chromosomes both to their sons and to their daughters. Half the sons and half the daughters get a 'black' X-chromosome (from the original mother), while half of them get a 'white' X-chromosome (from the original father). And half the sons have bar-eyes, half of them have normal eyes. All the children, whether male or female, that get an X-chromosome from the original father have bar-eyes, and all that do not have normal eyes.

This can be tested further by breeding many successive generations. This has been done; the matter has been tested in literally hundreds of thousands of cases. In every case, the results are such as above described. All the individuals, in any generation, that get an X-chromosome from the original abnormal parent, have the abnormal bar-eyes. All of those that do not get such an X have normal eyes. The bar-eye invariably follows the course of a particular X-chromosome and its descendants, appearing wherever that X-chromosome is present. This is a statement of positive fact, it is not theory; bar-eye follows a particular chromosome wherever it goes.

These experiments illustrate what is meant by substituting one chromosome for another. Examine the two kinds of sons in Fig. 10. Half of them have one kind of X-chromosome (black, that came from the original mother). The other half have another X-chromosome substituted for it, namely, the one that came from the original father (white). And this substitution changes the eyes from normal to bar-eyes. The same

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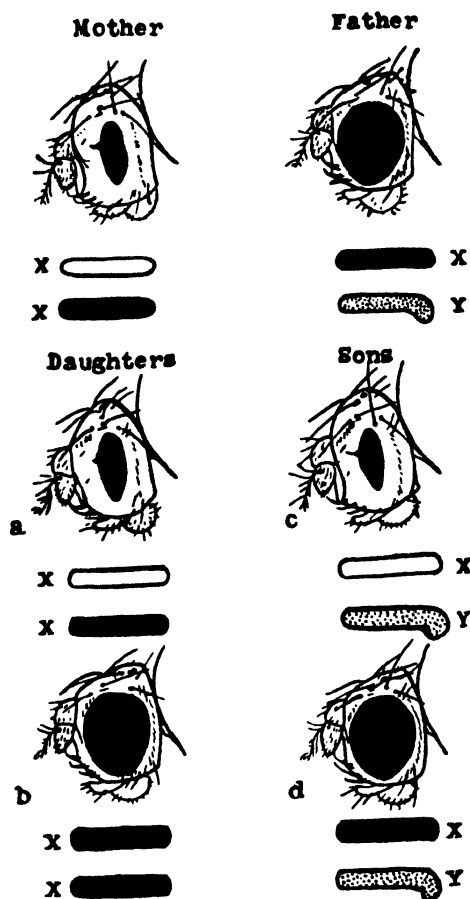


FIG. 10.—Inheritance of bar-eye when one of the daughters of Fig. 9 is the mother, while the father has normal eyes. The mother has one of the X-chromosomes that produces bar-eye (outline), one that does not (black), while the father's X is of the type that does not produce bar-eye. Of the daughters, half (a) receive from the mother the chromosome that produces bar-eye; half (b) receive the other chromosome; the former (a) have bar-eyes, the latter (b) do not. Also half the sons (c) receive from the mother the bar-eye chromosome, while the other half (d) do not; the former have bar-eye, the latter normal eye.

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substitution has been made in the case of the two kinds of daughters, with the same effect. Wherever an X-chromosome from the original father (white) is substituted for one from the original mother (black), the animal has bar-eyes. Wherever an X-chromosome from the mother (black) is substituted for one from the father (white), the individual has normal eyes instead of bar-eyes.

It is certain therefore that bar-eye is an abnormality resulting from a defect in certain X-chromosomes. It is clear that X-chromosomes can become defective, and that this change in the X-chromosome causes the individual to develop in an abnormal way, so that it possesses a bodily abnormality—in this case, an abnormality of the eye. This abnormality appears, as above seen, in any individual that has the defective X-chromosome, whether it also has a normal X-chromosome or not.

Dominant and Recessive Characters resulting from Substitution of Chromosomes.—The daughters produced in the experiment of Fig. 9 contain X-chromosomes from two different sources—one from the normal-eyed mother, one from the bar-eyed father. The one from the mother gives when by itself a normal eye, the one from the father a bar-eye. As the daughters have bar-eyes, it is evident that the effect of the chromosome from the father prevails over the effect of that from the mother. It is the custom to call the character that thus prevails and is manifested, when two chromosomes of different tendency are present, a dominant character. Thus bar-eye is dominant, as compared with normal eye.

Other X-chromosomes, in other individuals of *Drosophila*, are found to produce still other effects. Some are defective or abnormal, but instead of producing bar-eyes they produce other abnormalities. And most of them behave in a way that differs from the behaviour of bar-eye. An example will make clear this behaviour.

In certain cases X-chromosomes produce eyes that are white instead of red. Normally in the fruit-fly the eyes are red. But sometimes there are found individuals whose eyes are white. When these are mated together, they produce

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offspring all of whose eyes are white. So the white eyes are hereditary.

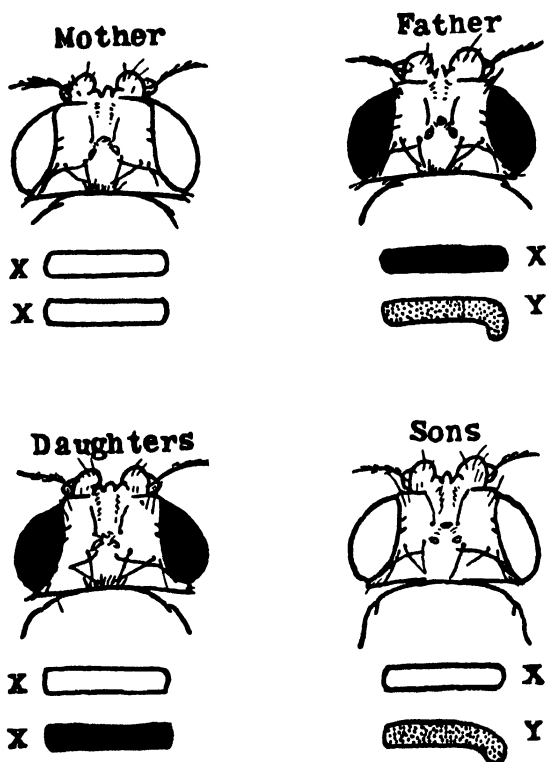


FIG. 11.—Inheritance of a recessive characteristic that depends on a particular type of X-chromosome: white eyes. The mother has white eyes, the father red eyes (represented in black). The X-chromosomes of each individual are represented below the figure of the head, the mother's chromosomes in outline, the father's in black. The daughters, receiving one X-chromosome from each parent, have red eyes, like the father. The sons, receiving an X-chromosome from the mother only, have white eyes, like the mother. The white eyes appear wherever the maternal type of X (outline) is the only type of X that is present.

But what happens if one mates together red-eyed and white-eyed parents? What will be the colour of the eyes in the offspring? Mate first a white-eyed mother with a red-eyed

DOMINANT AND RECESSIVE CHARACTERS

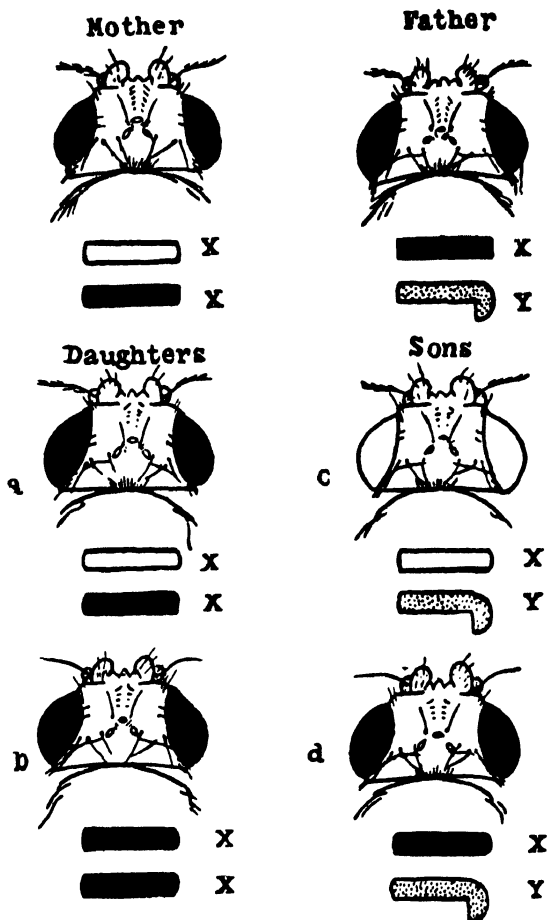


FIG. 12.—Course of inheritance of a recessive character (white eyes) that is dependent on a defective X. The mother has one defective X-chromosome (shown in outline), derived from the white-eyed mother of Fig. 11, her other X-chromosome being normal; she therefore has normal red eyes. The father has a normal X-chromosome (black), and normal red eyes. Of the four types of offspring shown (a, b, c, d), only one (c), representing half the sons, have the white eyes, this being the consequence of their receiving the mother's defective X-chromosome. All the daughters (a and b) and the other half of the sons (d) have normal red eyes, since they contain at least one of the normal X-chromosomes.

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father (Fig. 11). In this case the figure represents the mother's X-chromosome in white (since these are the abnormal individuals), while the father's are shown in black. Thus the descendants of the two kinds can be traced in later generations.

The sons get an X-chromosome from the mother only. And they all have white eyes, like the mother. The daughters get one X from the mother, one from the father. And they all have red eyes, like the father.

So the white eyes go with the mother's X-chromosome. But if one of the father's X-chromosomes is likewise present, then the white eyes are not produced; such daughters have red eyes. So the red eyes are dominant. The white eyes, since they do not appear if a normal X-chromosome from the father is present along with the abnormal one from the mother, are said to be recessive. White eyes appear only in individuals in which the abnormal X-chromosomes are the only kind of X present.

All this can be tested in a great number of ways. Mate, for example, one of these daughters, having the two kinds of chromosomes, with a normal red-eyed male, having a normal (black) X (see Fig. 12). Now half of the offspring get from the mother a defective X (white), the other half get from her a normal X (black). This is true both for the daughters and the sons. But the daughters get also a normal X from the red-eyed father. So they all have normal red eyes. But the sons do not get an X from the father; the only X they have is the one from the mother. And those that get the normal X from the mother have red eyes, while those that get the defective X have white eyes. That is, there is now produced a family in which all the daughters have red eyes, while half the sons have red eyes and the other half have white eyes. In a family of two hundred, there are a hundred red-eyed daughters, fifty red-eyed sons, and fifty white-eyed sons. The white eyes are present in all cases where the defective chromosome from the grandfather is the only kind present.

There are many ways to test this, and it is always verified. For example, if we cross one of the red-eyed mothers that has

DOMINANT AND RECESSIVE CHARACTERS

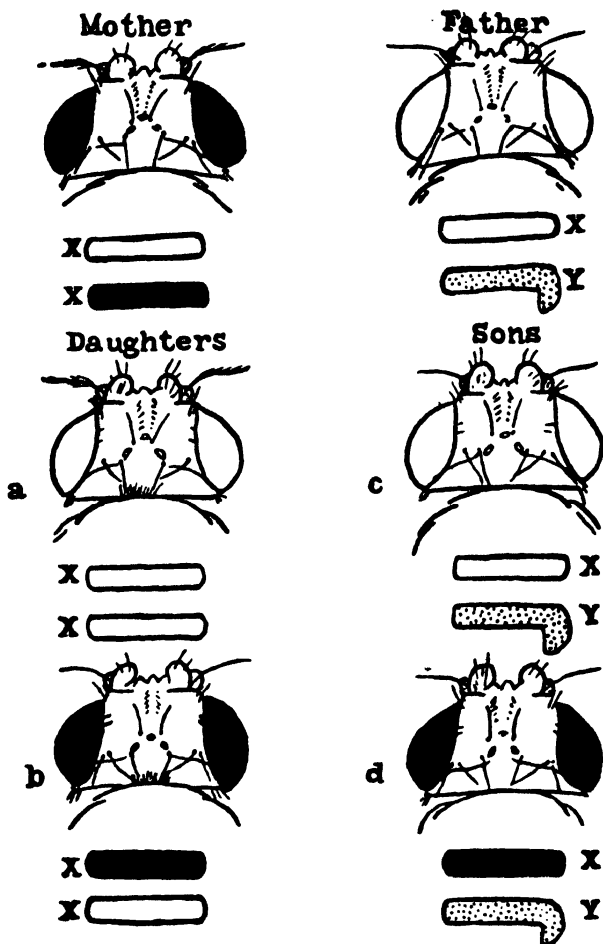


FIG. 13.—Course of inheritance of white eye and red eye in *Drosophila*, when the father has white eyes, and the red-eyed mother has one of the defective X-chromosomes (shown in outline) that tend to produce white eyes. Of the daughters (a and b), one half (a) receive a defective X-chromosome from both mother and father; these have white eyes. The other half (b) of the daughters receive a normal X-chromosome from the mother, a defective one from the father; these have red eyes. Of the sons (c and d), one half (c) receive the mother's defective X-chromosome and therefore have white eyes; the other half (d) receive the mother's normal X and so have red eyes.

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one defective X-chromosome, with a white-eyed father that also has the defective X-chromosome (Fig. 13), then we find that half the sons, and also half the daughters, have white eyes, the other half red eyes. And this is exactly the result given if the white eyes appear only where the defective X is the only kind present.

Since such characters appear in all males that have the defective X (since they have no other), while in females they appear only if both the X's are defective, they are much commoner in males than in females, and are, hence, often called sex-linked characters. But they appear in females as well as in males, provided that both the X's are defective.

Many Types of X-Chromosomes exist.—Thus it is clear, up to this point, that there are among the different individuals of the fruit-fly at least three kinds of X-chromosomes, with different effects. Some are normal, producing normal red eyes. Others have become defective in such a way that they produce bar-eyes. Others have become defective in such a way that they produce white eyes.

These are not the only kinds of changed X-chromosomes. Many different sorts of peculiarities have been found that thus follow the distribution of a particular type of X-chromosome, being manifested in the body of the individual when that type of X is the only type present. Up to 1925, a hundred and thirty diverse types of X-chromosomes had been detected scattered among the different individuals in the fruit-fly—each type giving rise to some special peculiarity. Many are known also in other organisms. In man a considerable number are known, giving rise mainly to defects or diseases. Among the characteristics dependent on changed X-chromosomes in man are some types of colour-blindness, also a blood disease known as haemophilia. They follow exactly the distribution of a particular type of X-chromosome. This, of course, shows that in man too the male has but a single X-chromosome, while the female has two, for this is the only way in which that method of inheritance can be brought about.

Thus it is established that when one X-chromosome is sub-

MANY TYPES OF X-CHROMOSOMES EXIST

stituted for another, this commonly makes a difference in the characteristics of the individuals. Since there are many types of X-chromosomes distributed among the individuals of a single species, such substitutions can be made in many different ways, giving many different types of results. In the fruit-fly, some X-chromosomes produce red eyes, others produce white eyes, others buff coloured, or eosin coloured, or various other coloured eyes. Some X-chromosomes produce long wings, others short wings—and so one could list a hundred or more diverse kinds of effects of diverse X-chromosomes. Similar long lists could be made for certain other organisms, and a considerable number of diverse types of X-chromosomes are known even in man.

The other chromosomes present somewhat more complex conditions than do the X-chromosomes, because they are always in pairs, while in some individuals (males) X is single. This makes detection of the effects of substituting one chromosome for another more difficult. But the same type of experimentation illustrated above for the X-chromosomes demonstrates that the other chromosomes also influence the characteristics of organisms. These matters are taken up in detail in later chapters.

It is clear therefore that the chromosomes are indeed 'materials of heredity'. That is, they influence the characteristics of the individuals that contain them, for these characteristics are altered when one chromosome is substituted for another. We turn next to a study of these materials.

NOTES AND REFERENCES ON CHAPTER I

1. Page 36. The relations between the materials of heredity and the characteristics of the organism have been far more thoroughly investigated in the fruit-fly, *Drosophila melanogaster*, than in any other organism, so that much of the detailed knowledge of these matters is based upon this animal. Most of the fundamental work on *Drosophila* has been done by T. H. Morgan and his associates, C. B. Bridges and A. H. Sturtevant, though in recent years many investigators in all parts of the world have been at work on the genetics of this organism, adding greatly to our knowledge. A

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detailed account of the genetics of *Drosophila* will be found in the following:

T. H. Morgan, C. B. Bridges and A. H. Sturtevant (1925), 'The Genetics of *Drosophila*', *Bibliographia Genetica*, vol. 2, pp. 1-262.

The detailed investigations of these authors are published for the most part in the publications of the Carnegie Institution of Washington. Among the more important are the following:

T. H. Morgan and C. B. Bridges (1916), *Sex-linked Inheritance in Drosophila*, Carn. Inst. Publ. No. 237. 87 pages; T. H. Morgan, C. B. Bridges and A. H. Sturtevant (1919), *Contributions to the Genetics of Drosophila melanogaster*, Carn. Inst. Publ. No. 278. 388 pages; C. B. Bridges and T. H. Morgan (1923), *The Third Chromosome Group of Mutant Characters of Drosophila melanogaster*, Carn. Inst. Publ. No. 328. 251 pages; A. H. Sturtevant, C. B. Bridges, T. H. Morgan, L. V. Morgan and Ju Chi Li (1929), *Contributions to the Genetics of Drosophila simulans and Drosophila melanogaster*, Carn. Inst. Publ. No. 399. 296 pages.

2

THE GENETIC SYSTEM

Its History during the Life of the Individual and in the Production of the Next Generation

IN Chapter 1 were described the discovery of the materials of heredity, and the methods by which it was proved that they do indeed affect the characteristics of organisms. These materials, it was shown, lie in the chromosomes. And it was seen that removing a chromosome, or substituting one for another, has great and varied effects on individuals.

The study of genetics is very largely therefore the study of these materials, and particularly the study of their physiological action, in reproduction and heredity. As a foundation for understanding their action, it is necessary to have clear ideas of the main features of their location and history, from the formation of the new individual, through its development to an adult, and thence to the formation of a new generation. This forms the subject of the present chapter. Though here heredity, variation and characteristics are not explicitly considered, it will be found that for their understanding, as taken up in later chapters, knowledge of the matters set forth in this chapter is essential.

The materials of heredity are gathered into a system of structures, which we may call the Genetic System. This system lies within the cells, and is as well defined in its constitution and functions as is the nervous or muscular system. It includes the chromosomes; whether it includes also other parts lying outside the chromosomes will be considered later. For the present it is the chromosomes that will be followed through the life of the individuals, since it is known positively that these effect the development and characteristics of

organisms. They will be traced, as material bodies, throughout the life of the individual, and into the next generation. Understanding of the action of the genetic system is largely dependent on having a clear picture of these matters.

To present this history clearly and systematically it will be best to set forth the main facts in a series of propositions, which will be further emphasized by giving to each a number or letter. We begin at the earliest condition of the young individual; that is, at the fertilized egg before it has divided.

A. The Genetic System in the First Stage of the Individual; the Fertilized Egg

1. As the new individual begins its separate life in the form of a fertilized egg, it contains, embedded in the cytoplasm of the cell, two nuclei, each with a set of chromosomes (Fig. 14).

2. One of these nuclei is from the mother (the 'female pronucleus'), the other from the father (the 'male pronucleus').

3. The two pronuclei contain the same number of chromosomes (or that from the father contains one less; see the following). The number contained differs in different organisms; it will be convenient to call the number n . Thus each of the two pronuclei has a set of n (or $n-1$) chromosomes, and the entire egg has two sets, making $2n$ (or in the male, $2n-1$) chromosomes.

The number n , present in each of the two pronuclei, is known as the *haploid* number. The number $2n$ (or $2n-1$), present in the two together, is known as the *diploid* number. In different organisms the haploid number varies from 1 to more than 100.

4. In some of the fertilized eggs (those that will develop into males), in some organisms, the pronucleus from the mother contains one more chromosome than that from the father. This additional chromosome is known as X. In the eggs that are to produce females (in these same organisms) the two pronuclei contain the same number of chromosomes, each having an X.

5. In organisms in which the number n is the same for both

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pronuclei, frequently in the eggs that are to produce males one chromosome (X) in the maternal pronucleus is larger than the corresponding chromosome (Y) in the paternal pronucleus.

6. In some organisms the different chromosomes in each single pronucleus differ much in size and shape (as in Figs. 3 and 7).

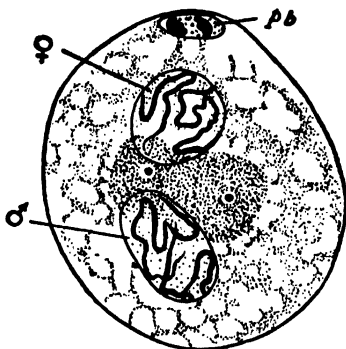


FIG. 14.—Fertilized egg of *Ascaris megalocephala*, showing the two nuclei, one from the father, one from the mother. After Boveri, from Wilson. Each nucleus contains two large chromosomes.

7. But the set of chromosomes in one of the two pronuclei is like the set in the other, as to size and form of the chromosomes, except in the case of the X and Y chromosomes above mentioned (see Figs. 4 and 5).

8. The two pronuclei are at first separate; they approach one another, come in contact, their membranes dissolve, and the two groups of chromosomes come closer together, forming a single group of $2n$ chromosomes (or $2n-1$). This is the diploid group.

9. Later this group becomes surrounded by a single membrane, constituting thus the single nucleus of the fertilized egg, containing the diploid number of chromosomes.

10. Thus in the single nucleus of the fertilized egg, half of the chromosomes are from the mother, half (or one less) from the father (Figs. 4 and 5).

11. Sooner or later the corresponding chromosomes of the

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paternal and maternal sets mate or conjugate, forming a pair. In some animals, as in the flies, this pairing of the chromosomes takes place soon after the union of the two pronuclei (in the 2-cell stage).

12. Thus the nucleus of the fertilized egg contains n pairs of chromosomes, one member of each pair paternal in origin, the other maternal.

13. In some organisms (the flies and others), the two chromosomes of a pair (maternal and paternal) remain paired throughout the life of the individual, and in all his cells.

14. In other species the two members do not pair till later (when germ cells are formed). But finally they mate, in practically all organisms.

We shall later examine what happens in mating of the chromosomes.

15. Even in species in which the maternal and paternal members are not at all times side by side, it is often possible to determine under the microscope which two chromosomes form a pair, since the pairs are of different sizes and forms, while the two members of the same pair are of the same size and form (Fig. 3).

The paired condition of the chromosomes turns out to be of great physiological importance.

B. The Chromosomes in the Cell Divisions that produce the Body

1. The egg divides into 2 cells, these into 4, and so on, to 8, 16, and the like, till a great number of cells are formed, making up the body of the adult organism.

2. At each cell division, each of the $2n$ chromosomes divides into 2, by splitting lengthwise (*mitosis*; see Fig. 2).

3. One half of each chromosome passes into each of the two cells formed by division.

4. There, each half grows to form a complete chromosome. Thus the chromosomes reproduce by fission, like Protozoa.

5. Consequently each cell formed contains the full set of $2n$ (or $2n-1$) chromosomes, half of them maternal, half paternal.

CHROMOSOMES IN THE CELL DIVISIONS

6. Ultimately therefore every cell of the body contains the set of $2n$ (or $2n-1$) chromosomes, half maternal, half paternal, in origin. (There are some exceptions to this statement.)

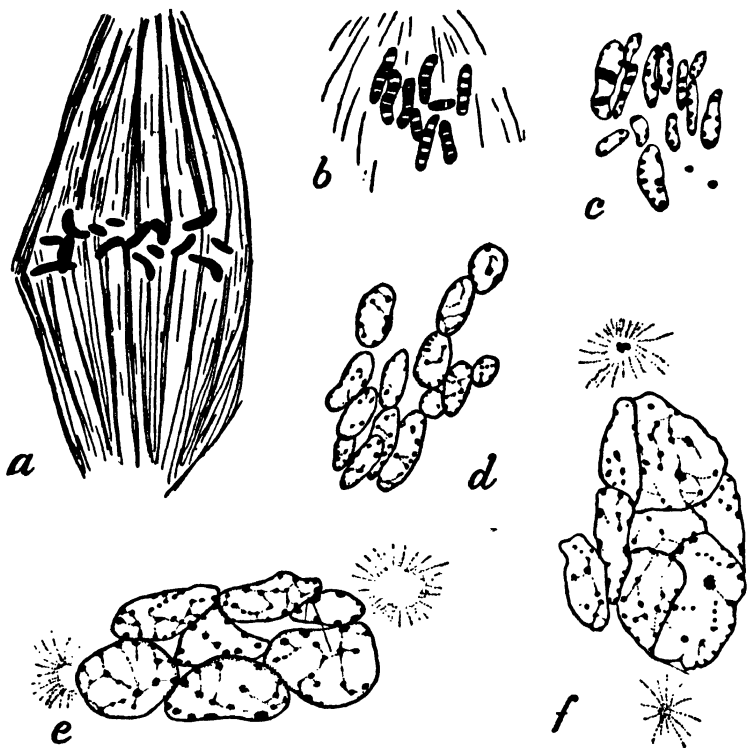


FIG. 15.—Transformation of the condensed chromosomes (a) by absorption of fluid into vesicles which slowly enlarge (b, c, d, e, f), finally constituting the nucleus. The figures show the process in the cells of the egg of a fish, *Fundulus*. After Richards.

C. The Chromosomes between the Cell Divisions, when the Cells are not Dividing

1. At the time of cell division the chromosomes are in the condensed condition (shown in Figs. 1, 3, 6, 7).
2. After completion of cell division, each chromosome

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absorbs fluid from the cytoplasm, grows, enlarges, and becomes a small vesicle.

This is a slow, gradual process, that can be seen under the microscope (see Fig. 15).

3. The vesicles become so large that their boundaries touch, and are pressed together, the boundaries becoming very indistinct or completely disappearing (Fig. 15, *e, f*).

4. The entire set of $2n$ (or $2n-1$) vesicles derived from the chromosomes constitutes the *nucleus* (what is called the 'resting nucleus').

5. In some organisms the entire set of $2n$ chromosome vesicles can be dimly seen and counted, even in this resting stage. In others this cannot be done.

6. As any cell gets ready to divide again, a new, small chromosome is laid down in each of the vesicles formed by the previous chromosomes.

7. When these new chromosomes first appear, they are usually irregular granules, which gather into a thread, having thickenings at intervals. In this condition they are called the *skein* or *spireme*.

8. These threads gather together and condense into the chromosomes of the type seen at cell division (Figs. 1, 2, 3).

9. The remainder of each large chromosomal vesicle dissolves in the cytoplasm of the cell. Here it doubtless produces chemical changes of importance.

Thus after every cell division the chromosome takes up a quantity of fluid from the cytoplasm, and later gives it off again, doubtless in modified form. This is probably one of the most important processes in development. It is presumably in this way that the chromosomes influence the development and the characteristics of the organism. They take up parts of the cytoplasm, change it, and give it off again. In this way are probably made the different kinds of tissues: muscles, nerves, bones, and the like. The chromosomes are thus continually active in the process of manufacturing the body (a matter to which we return later).

10. While thus in vesicular form, and active in the physiological processes of the cell, the chromosomes as such have in

CHROMOSOMES BETWEEN THE CELL DIVISIONS

most cases disappeared; they are no longer visible (though in exceptional cases they can still be detected). When later they reappear they show definite relations to the chromosomes that were visible before disappearance, in the following particulars:



FIG. 16.—Egg about ready to divide, formed by crossing two species of fish (*Menidia* by *Fundulus*). The two kinds of chromosomes are grouped separately; the long ones are from the *Fundulus* male, the short ones from the *Menidia* female. Enlarged from a figure by Moenkhaus (1904).

(a) The same number reappears. If the number is changed experimentally, as has often been done, it is the altered number that reappears.

(b) The chromosomes reappear in the same set of diverse forms and sizes as before. This is very striking in organisms like *Drosophila* (Fig. 7), in which the different pairs of chromosomes differ much. In hybrids, often the maternal and paternal sets differ greatly in size and form; each set reappears in its own type (Fig. 16).

(c) The chromosomes reappear in the original grouping

and arrangement. When the chromosomes that disappeared were in pairs, as in *Drosophila* they reappear paired as before. Often at disappearance the maternal and paternal sets are in two separate groups (as in Fig. 16); they reappear in these same groups. Often two particular chromosomes that are close together or intertwined reappear in this same condition.

Thus, even in cases in which the chromosomal vesicles are not separately detectable during the 'resting stage', it is obvious that each chromosome reproduces itself, in the same form, size, and position.

11. All this is repeated at every cell division (though the arrangement or relative position of the chromosomes gradually changes in the course of many cell divisions). Thus finally each cell of the body contains the complete set of $2n$ chromosomes, half from the mother, half from the father.

D. The production of Germ Cells, in relation to the Materials of Heredity. (See Fig. 17)

Having followed the main features in the behaviour of the chromosomes in forming the body of the individual, we next examine what happens when the individual reproduces: the processes in forming germ cells and in producing offspring. In dealing with heredity, it is particularly important to have these correctly in mind.

1. The individual begins as a single cell, the fertilized egg (B, Fig. 17).

2. It divides into many cells, some of which produce the body, while others produce the germ cells (C).

3. At an early stage in development there is usually among the numerous cells one that is later to produce all the germ cells; this is the primordial germ cell (Fig. 17, P).

4. The primordial germ cell in most organisms has the same set of chromosomes and genes as have the body cells. (There are exceptions to this in certain organisms.) That is, the primordial germ cell has n pairs of chromosomes, making $2n$ (or $2n-1$) chromosomes. Of these, n are maternal in origin, while n (or $n-1$) are paternal in origin.

THE PRODUCTION OF GERM CELLS

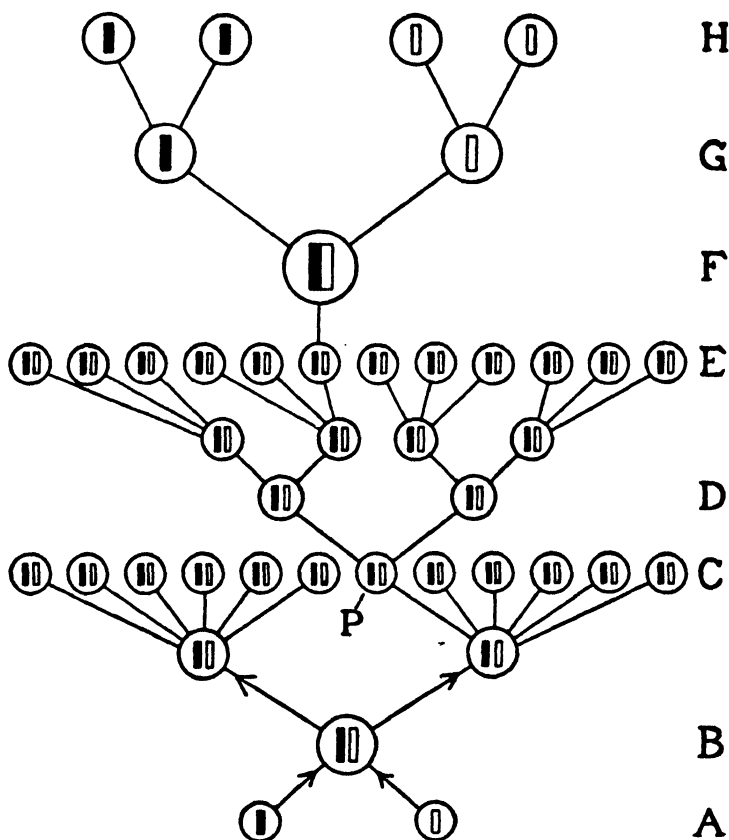


FIG. 17.—Diagram to illustrate the relation of body cells and germ cells, and the origin of both from the fertilized egg. Only a single pair of chromosomes is represented in each cell. At A are the two gametes (sperm and ovum) which unite to produce the fertilized egg B; each gamete contains one chromosome of the pair. The fertilized egg B divides, producing body cells C, among which is the primordial germ cell P. The primordial germ cell divides to produce many immature germ cells (E). The immature germ cell enlarges, the two chromosomes of a pair conjugating (F), then divides into four germ cells (G, H), each containing but one chromosome of the pair. (In the female three of the four germ cells (H) thus formed are not functional.)

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5. The primordial germ cell divides many times, to produce many immature germ cells. These still contain the full two sets, n pairs, of chromosomes (D, E, Fig. 17).

The immature germ cells in the male are the *spermatogonia*, while those in the female are *oogonia*.

6. There is usually a period of youth of the organism, in which the immature germ cells remain at rest, not dividing actively.

7. As the individual becomes mature, there is a renewed multiplication of the immature germ cells, the chromosomes remaining as before.

Next follows a series of processes by which the final germ cells are produced: in their totality they are known as maturation. They include important changes in the chromosomes; these changes taken together are known as *meiosis*. Maturation and meiosis include the following:

8. *Growth Stage*: Some of the immature germ cells now grow, becoming much larger (Fig. 17, F). After becoming large, the spermatogonia are called primary *spermatocytes*, while the oogonia are called primary *oocytes*.

9. Each primary spermatocyte and oocyte is later to divide twice, producing four mature germ cells.

While the growth and division are occurring, important processes occur in the chromosomes, as follows (see Fig. 18):

10. The chromosomes *pair* if they have not already done so; that is, the corresponding paternal and maternal chromosomes place themselves side by side close together.

11. While pairing, the chromosomes are in the form of very long slender threads, which have thickenings at intervals. There are corresponding thickenings side by side in the two threads (Fig. 18, A).

12. The two chromosomal threads (maternal and paternal) forming a pair become intimately united. This process is known as the conjugation, or synapsis, of the chromosomes. (During conjugation the two chromosomes may exchange parts, by 'crossing-over', as will be described later.)

This intimate union of the maternal and paternal chromosomes appears to be the ultimate act in the union of the sexes.

THE PRODUCTION OF GERM CELLS

13. Next occur certain processes, the general result of which is simple, although the processes are complex. The final result is that which would be produced if the immature germ cell now *divided but once into two final germ cells* and, in so doing, *the two chromosomes of each pair separated, one going to one of the two germ cells, one to the other* (Fig. 4). Thus each mature germ cell contains finally one chromosome (the maternal one or the paternal one) from each pair. The total number of chromosomes in the germ cell is now one-half the number originally present in the immature germ cell; it is n in place of $2n$. This is the process known as *reduction* of the number of chromosomes.

The actual processes are more complex, and are somewhat confusing. In following them, the final result just set forth should be kept in mind. They are as follows (Fig. 18):

14. During conjugation the two long chromosomal threads shorten and thicken (Fig. 18, A, B).

15. And while this is occurring, each of the two splits into two, so that there are now four partly united threads, two maternal, two paternal, in origin (see Fig. 18, C).

16. The shortening and thickening continues till the four threads have gathered into four closely united lobes (Fig. 18, D). These are known as 'groups of four', or 'tetrads'.

Since each *pair* of chromosomes becomes one tetrad, there are n tetrads. In each tetrad, two lobes represent a maternal chromosome, while two represent a paternal chromosome.

Some males have one chromosome (X) without a mate; this does not conjugate, but otherwise goes through the same process as the others, forming a two-lobed instead of a four-lobed body.

17. Now the large cell containing the n tetrads divides quickly, twice in succession ('maturation divisions'), thus producing four final germ cells (sperms or ova) (Fig. 18, E to J).

18. In these two maturation divisions, each tetrad divides twice, in such a way that the four lobes separate into the four different germ cells formed.

19. Thus two of the four germ cells receive from each tetrad a maternal lobe only, while two receive a paternal lobe only.

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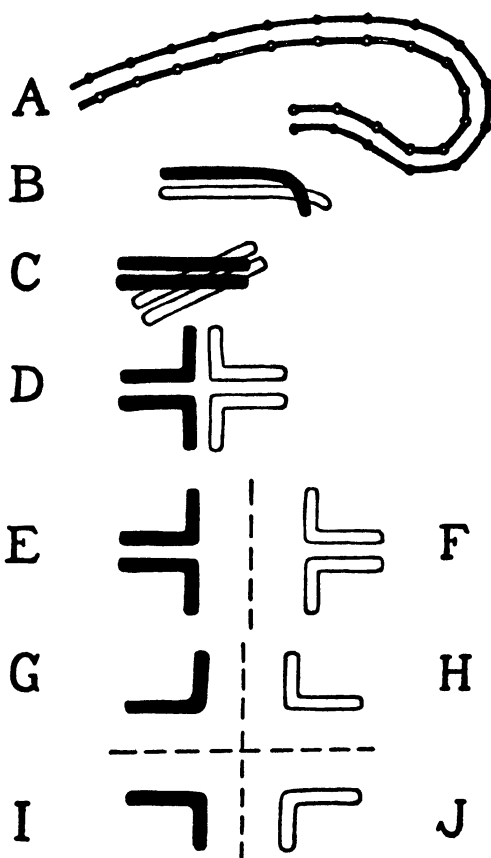


FIG. 18.—Diagram to illustrate the nature of the changes in a pair of chromosomes as germ cells are formed. *A*, The two chromosomes (one of paternal origin, the other of maternal origin) are paired. *B*, They have shortened and thickened. *C*, Each has split lengthwise. *D*, After further shortening and thickening, the four lobes are pressed together to form a tetrad. *E*, *F*, Cell division has occurred; two of the lobes have passed into the cell *E*, two others into the cell *F*. *G*, *H*, *I*, *J*, A second division has occurred; one lobe has passed into each of the four germ cells *G*, *H*, *I*, *J*, where they transform into chromosomes of the usual type. Thus each germ cell contains either the maternal or the paternal chromosome of the pair.

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20. These lobes transform each into a chromosome like that from which it was derived.

21. Thus each final germ receives either a maternal or a paternal chromosome from each of the n pairs that were present in the immature germ cells. Each therefore contains but n single chromosomes, in place of the n pairs (or $2n$ single chromosomes) that were present in the parental cells. This is the process of *reduction* of the number of chromosomes, from $2n$ to n .

As set forth in paragraph 13 above, the net result is the same as would be produced by the division of each immature germ cell into two instead of four, one chromosome from each pair passing into each of the two germ cells produced. For many practical purposes, one can think of germ-cell formation as occurring in this way (Fig. 4).

22. In the female, all the germ cells produced have the same number of chromosomes (n), since each receives an X chromosome. In some species, in which the male has an odd number ($2n-1$) of chromosomes, half the germ cells receive n chromosomes, the other half receiving $n-1$ (see Fig. 4).

23. In the male, all the four germ cells produced by the two maturation divisions are functional; they transform into *gametes*, known in the males as *sperms*.

24. In the female, three of the four cells formed by the two maturation divisions are small and without function; they are known as the polar bodies. The fourth is large, and is the functional gamete or *ovum*, which may be fertilized and may develop into a new individual.

25. A sperm with n (or $n-1$) chromosomes unites with an ovum containing n chromosomes, giving again a fertilized egg, or *zygote*, containing n pairs of chromosomes (Fig. 5).

26. Different germ cells from the same parent, and different fertilized eggs produced by the same two parents, receive different combinations of chromosomes. This results from the following facts:

(a) Each parent carries n pairs of chromosomes, one chromosome of each pair being maternal, the other paternal, in origin.

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(b) As we saw in the preceding chapter, the paternal and maternal chromosomes of a pair often differ in their effects. We may therefore designate them differently, calling one of them *A*, the other *a*, so that the pair is *Aa*.

(c) The chromosomes of the different pairs are often diverse in size and form; and, as will be shown later, they are also diverse in their functions.

Therefore we may designate the chromosomes of the different pairs by different letters. Thus the maternal chromosomes of the different pairs may be represented by the capital letters *A*, *B*, *C*, and so on, while the paternal chromosomes of the same pairs may be represented by the small letters *a*, *b*, *c*, and so on. The series of pairs in the cells of the parent are thus *Aa*, *Bb*, *Cc*, and so on, for *n* pairs (compare Fig. 5).

(d) As before seen, each final germ cell receives one chromosome from each pair. It may receive *A* or *a* from the pair *Aa*; *B* or *b* from the pair *Bb*, and so on.

(e) The different pairs are independent in their distribution to the germ cells. Thus from the two pairs *Aa* and *Bb* a given germ cell may receive any of the four combinations *AB*, *Ab*, *aB*, and *ab*; and similarly for other pairs. Any one combination occurs as frequently as any other.

(f) Thus with relation to one pair, as *Aa*, two types of germ cells are possible, *A* and *a*; similarly two types are possible from the pair *Bb*. Either type from *Aa* may be combined with either type from *Bb*, giving four diverse types from the two together, as illustrated above. Each additional pair multiplies the number of possible combinations by 2.

(g) Thus if the parent has *n* pairs of chromosomes, and the chromosomes of maternal origin differ in effect from those of paternal origin, the number of different types of germ cells producible as a result of this situation is 2^n , these having diverse combinations of chromosomes in the different germ cells produced by that parent.

Thus in *Drosophila melanogaster*, which has four pairs of chromosomes, the number of diverse types of germ cells that may be thus formed is 2^4 , or 16. If the four pairs are *Aa*, *Bb*, *Cc*, and *Dd*, then in the different germ cells there are such

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combinations as ABCD, AbCD, aBcd, aBcD, and so on. An organism with 10 pairs of chromosomes similarly produces 1024 diverse types of germ cells. In man, having 24 pairs of chromosomes, the number of diverse types producible is 2^{24} , or more than a million.

(As will be shown later, the number of diverse types of germ cells producible is greatly increased beyond these figures by the fact that the two chromosomes of a pair may during conjugation exchange parts in various proportions. See Chapter 6.)

27. Thus any single individual produces many diverse types of germ cells, containing diverse combinations of its chromosomes. This is true both for the sperms and the ova.

28. In fertilization, sperms and ova having the various diverse combinations of chromosomes unite at random. Thus the many fertilized eggs, and the offspring developed from them, bear different combinations of chromosomes. In consequence, as will be shown later, they may develop differently, giving many diverse types of individuals. The numbers of different types thus producible by a given pair of parents is dealt with in later chapters.

Certain Terms defined.—In connection with the above account of the history of the materials of heredity, it will be well to observe the meaning of certain common terms, whose use is very convenient; they will be employed in later pages:

Gametes: The mature germ cells (ova and sperm) are known as gametes. In the gametes the chromosomes are single instead of in pairs: that is, the gametes contain but n chromosomes, in place of $2n$. Cells having thus but one set of chromosomes are said to be *haploid*, while the usual cells, with chromosomes in pairs, are *diploid*.

The entire process of producing gametes is known as *gametogenesis*. The later processes, by which the four mature germ cells are produced, are spoken of as *maturation*. The chromosomal changes during maturation, resulting in reduction in the number of chromosomes from $2n$ to n , are known as *meiosis*.

Zygote: The fertilized egg, formed by the union of two

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gametes, is the *zygote*. This term is often applied to the individuals developed from the zygote. The zygote is diploid: its chromosomes are in pairs, their total number being $2n$. The union of the gametes to form the zygote is spoken of as the fertilization of the ovum.

Heterogametic: The individuals of one sex (the male in the types described above) form two kinds of gametes, one containing an X-chromosome, the other not. Such individuals are said to be heterogametic (or sometimes the term *digametic* is employed in the same sense).

Autosomes and Sex Chromosomes: The chromosomes X and Y, since they play a prominent part in the production of sex, are known as sex chromosomes. All the other chromosomes are known as autosomes. Thus *Drosophila melanogaster* (Fig. 7) has one pair of sex chromosomes and three pairs of autosomes.

NOTES AND REFERENCES ON CHAPTER 2

Extensive detailed accounts of the chromosomes, their history and activities, will be found in textbooks of cytology, such as the following:

E. B. Wilson (1928), *The Cell in Development and Heredity*, Third Edition, 1232 pp.; L. W. Sharp (1934), *Introduction to Cytology*, Third Edition, 567 pp.

3

OPERATION OF THE GENETIC SYSTEM, AS EXEMPLIFIED BY ITS RELATION TO SEX

Chapters 1 and 2 present as it were the framework of genetics. Chapter 1 gave the nature of the evidence which shows that the materials of heredity—the chromosomes—affect the characteristics of organisms. Chapter 2 presented a history of this material in the passage of generations. But the central problems of genetics lie in the physiology of this material. How does the genetic system operate in affecting the characteristics of organisms? And what are the phenomena of variation and inheritance to which it gives rise? To these questions we now turn.

Development and characteristics are affected in innumerable ways by the materials of heredity, as is shown by the results of substituting one chromosome for another. Among the most striking alterations so produced are changes of sex. A study of the relations of chromosomes to sex furnishes an excellent introduction to the physiology of the genetic system: it indeed leads far into the subject. The relations of chromosomes to sex will therefore be taken up first, and treated with some fullness, as revealing the nature of chromosomal action.¹

In Chapter 1 it was set forth that in many organisms the sex of the individual to be produced by an egg may be changed by altering the chromosomes which the egg contains. We wish to inquire how the chromosomes operate in producing sex differences.

1. Two groups of Organisms, having different relations of Chromosomes to Sex

In examining the question proposed in the preceding paragraph, we come upon the striking fact that in different groups of organisms there are very different relations of chromosomes to sex. There are two main groups, showing contrasted relations in this matter. One group, which includes the larger number of animals and plants, shows the relations that were described in Chapter 1. In these, the males have an unequal pair of chromosomes, X and Y (or they may lack completely the smaller chromosome Y), while in the females the corresponding pair consists of two equal chromosomes, XX. After this group had become known, the remarkable fact was discovered that there is another group of organisms, including the birds and some moths, in which this situation is reversed. In this second group it is the females that have the unequal pair of chromosomes, while the males have the corresponding equal pair. This is obviously a fact requiring consideration in all attempts to understand how the chromosomes operate in producing diversity of sex. The two groups may be characterized as follows:

Group I.—The males contain one pair of dissimilar chromosomes, X and Y; in some cases Y is lacking entirely. In addition they have a number of pairs, the autosomes, in which the two members of each pair are alike. The females carry an equal pair XX in place of the unequal (X + Y) pair of the males; they also have, of course, the usual autosomes. The conditions in Group I are represented in Fig. 3.

Thus in Group I the males are heterogametic, producing two kinds of sperms in equal numbers, one set of sperms bearing n autosomes plus X, the other bearing n autosomes without X—but in many cases with a Y. In the females all the gametes (ova) are alike as to their chromosomes—each containing n autosomes plus X. Sex is determined by the type of sperm that enters an ovum. A sperm of the constitution (autosomes + X) uniting with an ovum (autosomes + X) gives a

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female (2 sets of autosomes + XX). A sperm of the constitution (autosomes + Y) uniting with an ovum (autosomes + X) gives a male (2 sets of autosomes + XY). (In all such cases the Y may be lacking.)

To Group I belong many groups of organisms, including man. The following groups of animals are among those that show the relations of Group I: echinoderms, nematodes, molluscs, most insects, arachnids, myriapods, fish, mammals.

Four main subtypes may be distinguished in Group I, differing in the condition found in the males. These are:

Subtype 1. Male has X but no Y (Fig. 3).

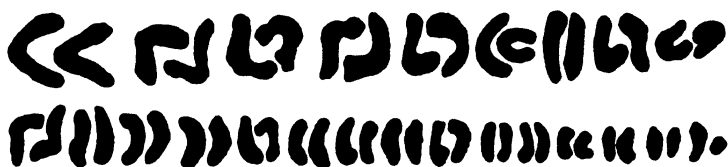


FIG. 19.—*The twenty-four pairs of chromosomes in man, arranged in order of size, after Evans and Swezy. The small unequal pair at the right end of the lower row are X and Y.*

Subtype 2. Male has a large X and a small Y (Fig. 6). To this group belongs man (Fig. 19). He has 23 pairs of autosomes, an X, and a small Y.²

Subtype 3. The male has an X, and a Y that is of different form and function from X (Fig. 7).

Subtype 4. The Y chromosome does not differ in form or size from X, but experiments of the kind to be described later show that it differs from X in function.

Other conditions, not classifiable under any of these four subtypes, occur in some organisms.

Group II.—The females have a pair of dissimilar chromosomes, in addition to the usual pairs of autosomes, while the males have a corresponding pair of similar chromosomes, in addition to the autosomes. The dissimilar chromosomes of the female are often called X and Y, as in the other group, while the similar ones of the male are called XX. But, by some

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authors, the dissimilar pair in this group are designated ZW, while the corresponding similar pair are ZZ.

In Group II, the females are heterogametic, producing two types of ova (autosomes + Z and autosomes + W). In the males, all the sperms are alike, with the constitution (autosomes + Z). The sex is determined by the type of ovum, not by the type of sperm, that enters into the fertilized egg. A sperm (autosomes + Z) uniting with an ovum (autosomes + Z) gives a male (2 autosome sets + ZZ). The same type of sperm (autosomes + Z) uniting with an ovum (autosomes + W) yields a female (2 autosome sets + ZW).

To this group belong birds and certain moths. The relations of the chromosomes to sex have been less fully studied in this group than in Group I.

2. Physiology of Sex Determination in Group I

The conditions in Group I have been extensively studied; they throw much light on the nature of the physiological action of the chromosomes, in their effects on development.

In Group I, as before seen, the males and females both contain in their cells two sets of autosomes (one set derived from each parent), and also an X-chromosome. They differ in the fact that the female contains an additional X, while the male has in place of this a Y; or in some species the Y is lacking entirely.

What part do these combinations of chromosomes play in producing the differences of sex? The way to determine this is to alter the chromosome combinations experimentally, and observe what differences this makes. This has been done extensively, originally by C. B. Bridges in the fruit-fly, *Drosophila melanogaster*.³ The results are of great interest; they will therefore be examined.

3. Alteration of the Chromosome Combinations in the Fruit-fly, and its Effect on Sex

It is important in following this work to have clearly in mind the chromosomal conditions in the organism used as an

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example. In this species of fruit-fly there are four pairs of chromosomes, three of them (II, III and IV in Fig. 7) being autosomes. In addition, the female has two large straight X's, while the male has one straight X and a hooked Y, of about the same size as the X (Fig. 7).

The autosomes as well as X and Y are important for sex, as it turns out. It will be convenient to indicate the three autosomes simply by the letter A. Thus the male produces two types of sperms, AX and AY, while the ova produced by the female are all alike, having the constitution AX. When the ovum AX is fertilized by a sperm AX, the result is AAXX, a female. But when the ovum AX is fertilized by the sperm AY, the result is AAXY, a male (see Fig. 5).

The Effect of changing the Numbers of X and Y Chromosomes present ('Non-disjunction').—Bridges discovered that sometimes, in forming the ova, an accident occurs of such a sort that the two X's do not separate into different ova, but both go together into one ovum, leaving another ovum without an X. Thus two kinds of ova are produced, AXX and AO (using O to signify the absence of X or Y) (see Fig. 20, at B).

This failure of the two X's to separate is called non-disjunction of the X-chromosomes. Later a race of fruit-flies was discovered by L. V. Morgan in which the X-chromosomes are stuck together, so that they almost never separate. In this race germ cells are practically always formed in the way just described. So it has been possible to study the results thoroughly, since thousands of offspring have been obtained. These results are of great importance and interest.

From such individuals we have then two kinds of ova, one AXX, with two X's; one AO, with no X (Fig. 20, B). What will happen when these unite with the usual two kinds of sperm, AX and AY?

When the ovum AXX unites with a sperm AY, we get offspring AAXXY (Fig. 20, B), containing two X's and also a Y. Will such an individual be a male or a female? The results show that it is a female.

This result shows at once certain important things about sex determination. (1) The presence of Y (found normally in

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males) is not sufficient to produce a male. (2) It is the presence of two X's, not the absence of Y, that yields a female. (3) The same sperm AY that would normally produce a male, yields a female if the ovum contains two X's.

When the ovum AO, without X, unites with a sperm containing X (that is, AX), we obtain a fertilized egg AAXO

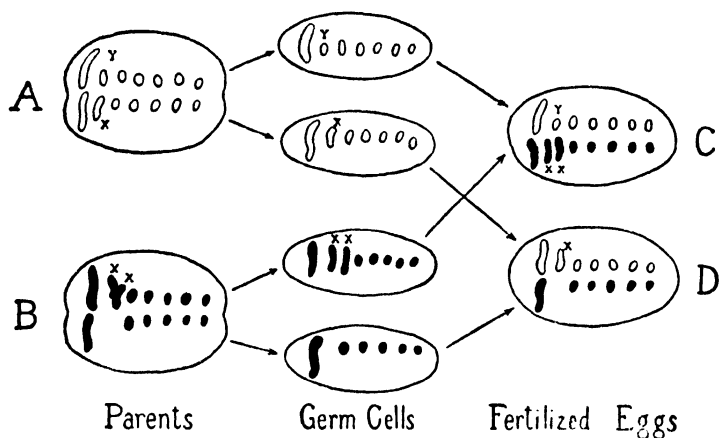


FIG. 20.—Diagram to illustrate the results of the failure of the two X's to separate, in the production of germ cells by the female. A, normal formation of germ cells in male, giving two sets of germ cells, one containing Y, the other X. B, non-disjunction in the female; the two X's fail to separate, giving two sets of germ cells, one containing two X's, the other with no X. C, female containing XXY. D, male, containing X but no Y.

that has but one X, and no Y (Fig. 20, D). What sort of an individual will this be?

Observation shows that this combination produces a male, although it has no Y. Certain other important points are thereby demonstrated. (4) The Y-chromosome is not required in order to produce a male. (5) It is the lack of one X that gives origin to a male. (6) The sperm that contains X, which normally produces a female, yields a male if it enters an ovum containing no X. (7) When the usual autosomes are present,

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two X's give a female, one X a male, whether the Y-chromosome is or is not present in addition.

Certain other combinations are produced. When an ovum AO, lacking X, unites with a sperm AY, containing Y but no X, the fertilized eggs AAY do not develop. (8) This shows that the presence of one X is necessary for development.

When an ovum AXX, with two X-chromosomes, unites with a sperm AX that also contains an X, the resulting individual AAXXX contains three X's, but only two sets of autosomes. The results are as follows: Most such individuals with XXX do not develop. A few develop, but are abnormal; development is disturbed by the presence of the additional X. The abnormality consists in an accentuation of the structural peculiarities that distinguish the females from the males. The individuals seem as it were to be more female than those containing but two X's. Bridges calls them super-females.

From these experiments we discover that when two normal sets of autosomes are present, lack of an X is fatal: the presence of one X causes the production of a male; two X's cause the production of a female; three X's give rise to an abnormal 'super-female'.

One further fact should be mentioned. The males containing a single X but no Y, while well formed, are sterile; they do not produce functional sperm. Thus the chromosome Y is not entirely without function; it is necessary for the production of normal male germ cells.

Still other combinations of chromosomes can be produced by mating together in various ways the different types of individuals just described. In the following list are given the various combinations that have been produced, with the nature of the individuals that they yield.

AAXY, normal male.

AAXX, normal female.

AAXXY, typical female.

AAXXXY, typical female.

AAXO, male, sterile.

AAYO, does not develop.

AAXXX, abnormal, 'super-female'.

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All of these results show that changing the number of X's present is what changes the sex, while changing the number of Y's does not change the sex.

In all these cases there are present two sets of autosomes, AA, in addition to the X's and Y's. Have these autosomes any effect on sex? What would happen if the numbers of autosomes were changed? To this question we now turn.

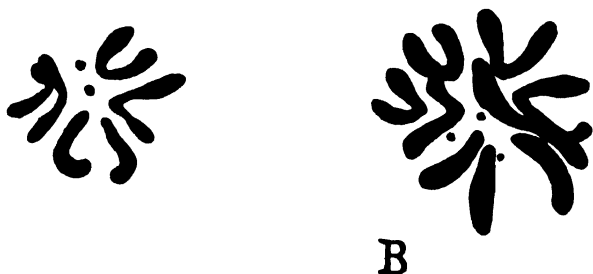


FIG. 21.—Chromosomes in diploid (A) and triploid (B) *Drosophila*, after Bridges (1922). In A is shown the normal condition in the female: four pairs of chromosomes. In B are shown the chromosomes of the triploid female: four groups of three chromosomes each.

The Effect of changing the Number of Sets of Autosomes present.—Bridges discovered further that sometimes the number of autosomes becomes changed, and he determined the results of such changes. In the normal individuals there are two sets of autosomes, one from each parent; that is, the chromosomes are in pairs, AAXX (Fig. 7). Certain individuals in the fruit-fly were discovered to have their chromosomes in sets of three instead of in pairs. Such individuals are known as triploids; their chromosomes may be represented as AAAXXX. How these individuals were produced is not known. It seems probable that in some way germ cells were produced in which the two chromosomes of the pairs did not separate, so that these germ cells were AAXX. These being fertilized by the usual sperm, AX, gave the triploids. It is important to understand that the existence of these triploids is determined under the microscope. Their chromosomes in microscopic preparations are seen to be in threes (Fig. 21).

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When such triploids form germ cells, some of the latter are of the usual haploid type, AX, while others have their chromosomes in pairs, AAXX; that is, they are diploid. Some of both types of course have Y-chromosomes in place of the X's, so that there are germ cells AY, AX, AAYY, AAXY, and AAXX. Such germ cells when they unite produce many different chromosome combinations, some with autosomes in pairs, others with autosomes in threes or even in fours; and with different numbers of X's and Y's. Many individuals having such combinations have been produced and studied. This has given opportunity to determine the effect of varying the numbers of sets of autosomes, as well as of varying the X's and Y's.

The more important different combinations, with the nature of the individuals produced, are given in the following list:

<i>Autosomes</i>	<i>Sex chromosomes</i>	<i>Result</i>
2 sets, AA	XX	Normal females
3 sets, AAA	XXX	Normal females
4 sets, AAA	XXXX	Normal females
3 sets, AAA	XX	'Intersex'
3 sets, AAA	XY	'Super-males'
2 sets, AA	XXX	'Super-females'

Here we find that while two X's normally give a female, if they are combined with three sets of autosomes they do not give a female, but an individual intermediate between the male and female; an 'intersex'. It is clear therefore that the autosomes influence sex, as well as do the X's. Furthermore, it is not the absolute number of autosomes present that gives a particular effect, but the number of sets of autosomes in relation to the number of X's. Three sets of autosomes with but two XX's gives an intersex, while three sets of autosomes with three X's yields again a normal female. The sex produced depends upon a balance between the autosomes and the X's. When the number of sets of autosomes equals the number of X's (whether two, three or four) a female is produced. When the number of sets of autosomes exceeds the

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number of X's, there is a tendency for males to be produced. Two sets of autosomes plus one X gives the normal male. Three sets of autosomes plus two X's yields a combination in which the proportional excess of autosomes is not sufficient to produce complete maleness; it yields intersexes. But when three sets of autosomes are present with but one X, the scale is tipped too far in the direction of maleness. Abnormal individuals are produced in which the characteristics that distinguish males from females are accentuated beyond the normal; Bridges calls these 'super-males'. And similarly, if three X's are present with but two sets of autosomes, the balance is tipped in the opposite direction, and 'super-females' are produced.

We may summarize the special results of these observations as follows:

(1) Both autosomes and X-chromosomes take part in determining the sex. Altering either class of chromosomes changes the sex.

(2) Which sex is produced depends upon a balance between the number of sets of autosomes and the number of X's.

(3) A preponderance of the number of X's tends to produce females; a preponderance of the number of sets of autosomes tends to produce males.

(4) By altering the balance in ways not commonly occurring, various intermediate and extreme conditions as to sex are produced.

4. Method of Operation of the Chromosomes in producing Sex Differences

The results just set forth are of great significance for the understanding of the method of operation of the chromosomes in development. Their bearing will best be appreciated by bringing out certain other relations that are found in the observations above described, on the relations of chromosomes to sex.

(1) As before seen, changing the number of X's, when the

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autosomes are left unchanged, changes the sex. Two XX's produce a female, one X a male.

(2) Thus the female XX contains everything that is necessary for producing a male. It differs in having 'two doses' of X in place of one. By removal at an early stage of development of one of these 'doses', it should be possible to transform the female into a male (see later, p. 85).

(3) The male, XY or XO, contains all the kinds of materials required to produce a female. It contains X, as does the female; but it has only 'one dose' of X in place of two.

It should be possible therefore to convert the male into a female if the single X-chromosome of the fertilized egg could be caused to divide into two, while the other chromosomes remained undivided, thus giving an individual with chromosomes AAXX.

(4) Thus males and females do not differ at the beginning by containing different kinds of materials. Both demonstrably contain the same kinds of materials. The difference lies in the fact that the female has two centres of growth and multiplication for a certain material (X), while the male has only one centre of growth for that same material. Such a difference is commonly spoken of as a difference in 'balance' among the chromosomes.

If this material (X) has a certain type of effect, the difference between a condition with two centres of action for that material, and a condition with but one, might well make a great difference to the chemical and physiological processes occurring. In every cell, throughout life, the processes in the female are such as result from the interaction of these two centres with the other cell contents, while in every cell of the male the result is that produced by the interaction of but one such centre with the other contents.

The result of this difference in balance of the chromosomes is in fact to produce the very great differences, structural, physiological, mental, that distinguish the female from the male. The fact that so many and so great differences, of so many diverse kinds, are brought about without any original difference in the kinds of materials present, but only in balance, only in the number of centres of growth for certain

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materials, is of the greatest significance for the nature of the processes of development; it should never be lost sight of in considering the facts of heredity. Other differences produced by diversity of chromosomes, to be taken up later, may perhaps be brought about in a similar way.

Through what Means do the Chromosomes produce Sex Differences?

How can differences between chromosomes produce such great differences as those shown by individuals of different sexes? What is their method of action in bringing about sex differences?

Although a complete answer to these questions cannot be given, much is known that bears on them. Many things have been discovered as to the means through which chromosome differences produce sex differences, and these things are most instructive for forming a conception of the nature of development and heredity.

Activity of the Chromosomes in Development

As before seen, the chromosomes are very active bodies. They are continuously working at the cytoplasm of the cells, interacting with it, changing it. In Chapter 2 this was described. In the very young cells, just after cell division, the chromosomes are small compact bodies. They begin to absorb material from the cytoplasm around them. They thus enlarge, becoming vesicles filled with substance. Each becomes doubtless a hundred times as large as before. In time the vesicles become so large that they are crowded together to form the large nucleus (Fig. 15).

What becomes of this large amount of fluid taken in by the chromosomes? It undoubtedly becomes chemically changed by interaction with the chromosomes. There is evidence of this in the chemical reactions of the material of the nucleus as compared with those of the cytoplasm, and in certain other processes that will be discussed later.

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The nucleus thus has filled itself with cytoplasm, which has been acted on, changed, by the chromosomes. Then, before the next cell division, it pours this altered material back into the cytoplasm. The outside membrane of the nucleus dissolves and all the materials pass out, except that there remains still a small concentrated chromosome, from each one of the former vesicles.

This taking in of cytoplasm, altering it, and giving it off again, is repeated at every cell division, so that it is continu-

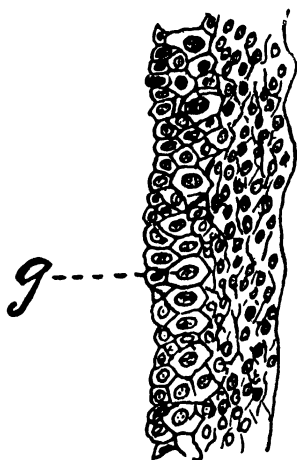


FIG. 22.—*A portion of the germ gland at an early stage in the pig, showing the enlarged genital cells (g). Redrawn from a figure by Nagel, in Hertwig's Handbuch der Entwicklungslehre.*

ously going on throughout development; it is occurring in every cell of the body. In this way the cytoplasm becomes gradually changed. Different kinds of materials are produced in the different cells; the different tissues and organs of the body are thus ultimately formed.

Thus it might be expected that sex differences would be produced through the fact that different chemical reactions occur when the cells contain but one X, from those that take place when two X's are at work. And there is proof that this is true. To illustrate these matters, we may summarize

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what happens in the development of sex differences in mammals.

(1) In mammals the two sexes differ at the beginning of their lives, in the fertilized egg, as to the number of X-chromosomes they contain. Both contain the usual two sets of autosomes; in addition the female has two X's, the male but one X. What difference in development does this make?

(2) At first the two sexes develop alike, so far as can be seen, so that the individuals are in an 'indifferent' condition, with respect to sex.

In this indifferent condition, the embryos develop so far that head, limbs and all systems of organs are distinguishable: in the rabbit this condition is said to continue for about 14 days.

(3) While in this indifferent condition, certain cells are set off as germ cells. These are gathered into a strip of small cells called the germ gland, lying on the dorsal surface of the body wall (Fig. 22). Some of the small cells become much larger than the others; these are called genital cells. The genital cells are to produce later the new germ cells (sperm or ova) of this individual. They are alike in the two sexes (except as to their X-chromosomes of course).

(4) Now the germ glands in individuals of which the cells contain but one X—in the males—begin to develop in a distinctive fashion: the cells arrange themselves in 'cords' and take on a characteristic appearance. At the same time the germ glands of individuals whose cells carry two X's—the females—remain in the indifferent condition. Later, in the males the genital cells divide into small cells, which become the mother cells of the sperms; while in the females they enlarge, later to produce ova. These differences in development are due directly to the fact that one set of cells contains a single X, the other set two X's.

As seen above, there is a period in which the male has developed distinctive characteristics, while the female is still in the indifferent condition. This turns out to be a matter of importance, as will be brought out later.

(5) The two sexes continue to develop differently to adult life. The male germ gland becomes the testis, which produces

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sperms; and the body of the male develops differently from that of the female, producing the male secondary sex characters (mane, beard, greater size and the like). The female germ gland becomes the ovary, which produces ova; and the body develops the female secondary sex characters (mammary glands, diverse body form and size and the like).

Thus the male and female have become very diverse, differing in a great number of ways, both structurally and physiologically.

All these later differences result in some way from the original difference in the X-chromosomes: from the presence of but one X in one set of individuals, of two X's in the other. Our present question is: through what means does the chromosome difference produce the later differences?

The answer to this question is approached through a series of experiments, the results of which we may summarize:

(6) *Experiment.*—Remove the germ gland (testis or ovary) from the very young individual, before the later sex differences are produced.

The result is that the later sex differences do not appear. Both sexes remain nearly or quite in the indifferent condition, so far as sex differences are concerned, though they continue to grow and develop in other ways.

(7) It follows *that the later sex differences are produced through the action of the germ glands* (ovary or testis). The body cells of the two sexes still retain the differences as to the number of X-chromosomes present, but without the germ glands this does not result in the production of the later sex differences.

How do testis and ovary act in producing the later sex differences? This is tested by another experiment:

(8) *Experiment.*—Interchange the germ glands of the two sexes. Remove the ovary from a young female, and replace it by transplanting to the female body a testis taken from a young male (Fig. 23, A).

Similarly, remove the testis from a young male and replace it by an ovary taken from a young female (Fig. 23, B).

These experiments are difficult, but have been successfully carried out in rats by a number of investigators.

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Result.—The female body (XX) containing a testis (XO) develops the male secondary sex characters! The male body (XO) containing an ovary (XX) develops the female secondary sex characters (such a male develops a mammary gland that may produce milk; it may suckle the young).

(9) The results of the experiments show that it is the nature of the germ gland (whether of the XX or the XO type) that determines (mainly or entirely) what later sex characters

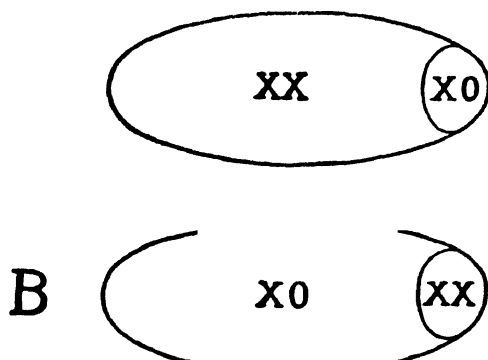


FIG. 23.—Diagram of the experiments in exchanging germ glands. A, female body XX (having a pair of X's in each cell) containing a male germ gland XO (having but one X in each cell). B, male body XO (having but one X in each cell) containing a female germ gland XX (with two X's in each cell).

shall be produced. A body whose cells contain but one X will produce either male or female secondary sex characters, depending on whether it contains a germ gland having cells of the constitution XO or cells of the constitution XX. And the same is true for the body whose cells bear two X's.

(10) By what means do the germ glands affect the development of the body?

The germ gland is small and located at a definite place in the body. The secondary sex characters appear in many parts of the body, often situated far from the germ gland. Thus the germ gland influences parts at a distance from itself. How is this done?

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(11) The suggestion that comes most readily to mind is that each type of germ gland produces a characteristic secretion, which passes throughout the body and influences the development of all parts. The secretion from the testis (XO) would thus produce one type of development (toward the male), the secretion from the ovary (XX) another type. Such suggestions have often been made.

(12) Confirmation of the suggestion of diverse secretions circulating in the body: the 'freemartin'.—When twins of opposite sexes occur in cattle, the male twin is a normal, well-developed male. But the female twin is usually an 'intersex'; it is intermediate in structure between the male and female. It has many male characteristics, together with some female characteristics. There are different grades of intermixture, in different cases, and sometimes the female is normal.

What is the cause of this partial transformation of the female into a male?

It was found by F. R. Lillie⁴ that in all such cases there is an intercommunication of the blood system of the two twins, so that blood flows from the body of the male twin into the body of the female, and vice versa. But, in cases where the female is normal, there is no intercommunication of the blood systems.

From this it appears clear that the cause of the partial transformation of the female into a male is this intercommunication. Blood flows from the body of the male into that of the female, causing the latter to develop in the direction of maleness.

But why should it change the female only, not the male? Why does the latter not become intermediate also?

The answer to this question is given, with great probability, by the fact noticed on an earlier page, that the male begins the development of its distinctive sexual characteristics earlier than does the female. The individual is recognizable as male, before the female changes from the juvenile condition. Hence the male begins to produce its characteristic secretion first. This then circulates into the female body, and transforms it in the direction of maleness. As a result the female never pro-

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duces its characteristic secretion, and so the male is not influenced.

Such secretions circulating in the blood, and influencing development, are known as *hormones*.

Can such male and female hormones be extracted from the blood, and used experimentally to produce male or female characteristics? This has been done to a certain extent. The hormones have not yet been obtained in a pure condition. But enough has been done to show that male and female hormones do exist, that they circulate in the body, and that they affect the sex characteristics.

(The account given above relates to mammals. In birds also sex hormones have been discovered, playing a rôle similar to that of the sex hormones in mammals, though with some striking differences. In insects, on the other hand, hormones do not appear to play a part in producing sex differences.)

The Question answered: The Means by which the Chromosomes affect Sex

The facts just summarized as to sex development in mammals provide a general answer to the question as to the method of operation of the chromosomes in determining sex. The answer is that the chromosomes determine sex by altering the chemical processes that occur in development. The cells bearing XX produce a secretion that differs in its physiological effects from that produced by the cells bearing XO. These two diverse secretions bring about the different developmental processes that result in the production of the two sexes.

As before seen, the difference in the secretions or hormones results in some way from the fact that the XX cells have two centres for the production of certain materials, while the XO cells have only one centre for the production of those materials. The different proportions of materials result in diverse chemical processes that give the two different hormones, and thus result finally in individuals of different sex.

POSSIBLE WAYS OF DETERMINING SEX

May other Things besides the Chromosomes influence or determine Sex?

We have gone into the matter of sex determination primarily for the purpose of getting light on the method of action of the chromosomes. We have seen that the nature of the chromosomes present affects the chemical and physiological processes of development, and in this way determines which sex shall be produced.

This suggests certain other questions regarding sex that it will be well to examine briefly. It is commonly said that sex is determined by the X-chromosomes (a true statement so far as it goes); and from this it has often been concluded that sex cannot be determined in any other way. In particular it has been held that this excludes the possibility of the determination of sex by particular environmental conditions.

This conclusion is, however, quite without justification. The fact that chromosomes determine sex does not prevent other things from determining it. The chromosomes determine sex only in the sense that changing the chromosomes alters the sex. We have already seen that changing other things likewise alters sex. Changing the X-chromosomes alters sex; changing the autosomes alters sex; changing the germ glands present alters sex; changing the hormones present alters sex. It will be worth while to enumerate various different ways in which sex could be determined, in view of our knowledge of the method of action of the chromosomes. Some of the ways are known to be realized; others are not as yet known to occur.

Summary of Possible Ways of determining Sex

1. Selective action exercised on the germ cells containing particular chromosomes.—In the organisms of Group I, there are two kinds of sperms; those containing an X-chromosome (which produce females), and those containing no X (which produce males). Any agent that would determine whether certain eggs are fertilized by an X sperm or by one without

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an X would determine the sex. There are a number of possibilities of this sort.

(a) It is known that the sperms containing an X-chromosome are in some animals larger than those without X. It may well be, therefore, that one kind of sperm is more vigorous and active than the other. This kind would then fertilize a greater proportion of eggs than the other, so that a majority of the offspring would be of one sex rather than the other.

There are indications that something of this sort is true in certain organisms. Males and females are not produced in equal numbers in all organisms. The average number of males to every 100 females are for certain species as follows:

Man 105, Cattle 107, Pigeon 115, Cottus (fish) 188, Lophius (fish) 385, Squid 17, Octopus 33. (Data from Goldschmidt, 1923).

Such disproportion between males and females might also be produced in some of the other ways hereinafter mentioned.

(b) It is known that in some organisms all the sperms of one type die. In a species of Phylloxera, according to Morgan,⁵ at a certain period in the life history all the sperms that do not contain X die. As a result, all of the offspring produced in the next generation are females.

(c) If one of the two types of sperm is more resistant than the other, certain unfavourable conditions might injure or destroy one type and not the other. As a result, all or most of the eggs would be fertilized by the uninjured type of sperms. Then all (or most) would produce individuals of the same sex. If the sperms with X were the ones injured, then all the offspring would be males; in the alternative case, all the offspring would be females.

Such effects might be produced by conditions of temperature, or chemical conditions, or by certain elements in the food of the parent. It would then be found experimentally that these conditions 'determine sex'. Whether such effects are actually produced is to be discovered only by observation and experiment.

(d) The eggs might have such chemical or physical properties as to admit one of the kinds of sperm, not the other.

POSSIBLE WAYS OF DETERMINING SEX

This would determine what sex is produced. There are indications that something of this sort occurs in some organisms.

(e) Certain chemical or physical conditions of the environment might alter the properties of the egg, making it admit one type of sperm, not the other. Such environmental conditions would then determine the sex to be produced.

2. Destruction or division of an X-chromosome.—Anything that would destroy one of the X-chromosomes in a fertilized egg containing two X's would determine the sex: the individual produced would be a male instead of a female.

There is strong evidence that such transformation of an individual that began as a female into a male (wholly or partly) occurs at times. There occur in insects individuals in which one half of the body is female, the other half male. In some animals it is easy to detect this, because the males and females differ in structure or colour in all parts of the body. Such individuals are known as gynandromorphs. In *Drosophila*, individuals are found at times in which one half of the body, to the middle line, is of one sex, the other half of the other sex. Such individuals would be produced if, in an egg containing two X's, in the two-cell stage an X were lost from one of the two cells, but not from the other. The half retaining the two X's would remain female, while the other half would become male.⁶

Loss of a chromosome in the process of cell division has been observed in certain cases. One of the chromosomes becomes entangled with the advancing cell wall, as the cell divides; it is thus removed from the cell. If this happened to the X-chromosome in one cell of the two-cell stage in *Drosophila*, a gynandromorph would be produced.

Sometimes individuals are found in which three-fourths of the body is female, while one-fourth is male; or in other cases nearly the whole body is female, while a very little is male. Such conditions would arise if one X-chromosome were lost from a cell at a later stage of development.

Gynandromorphs might also be produced if by some means the X-chromosomes of certain cells containing but one X could be caused to divide, while the other chromosomes

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remained undivided. There are no cases known in which this appears to be the method of action. Gynandromorphs occur in birds as well as in insects, but are not known in mammals.

3. Changes in the chemical processes occurring in the cell.—We know that the chromosomes affect sex by influencing the chemical processes in the cells. Any agent that influenced these chemical processes, in the same or a reverse way, would determine which sex would be produced. As before seen, it would be necessary only to alter the balance of the chemical processes occurring. An agent that in *Drosophila* reinforced the action of the autosomes would turn the development in the direction of producing a male. An agent that increased the chemical action produced by the X-chromosomes would tend to cause the production of females.

These considerations open the door to many possibilities; since in the chromosomes we are dealing with centres of chemical action, these might well be favoured or hindered by various conditions. Changes in the chemical processes might well be induced through the action of certain types of nutrition, through temperature changes, through reactions to various stimuli, and the like. Whether such conditions determine sex is to be discovered only by observation and experiment; there is nothing in the known method of action of the chromosomes to prevent.

4. In some organisms the sex of the individual is known to be determined by the conditions under which it develops. Examples of this are the following:

(a) In a certain common mollusc called *Crepidula plana*, if the eggs are kept away from full-grown individuals, they develop into females. But if they are allowed to develop near to older specimens of *Crepidula*, they become males. In such eggs there is thus a very delicately balanced condition, which may be turned toward either sex by a slight change of conditions.⁷

(b) In a marine worm known as *Bonellia*, the female is a large worm with a proboscis. The male, on the other hand, is very small, and is parasitic within the body of the female (in the uterus). The eggs develop into small creatures that swim

DIFFERENT CONDITIONS AS TO SEX

about in the water. If they find a female, they attach themselves to her proboscis and develop into males. But if they do not become attached to a female, they themselves develop into females.

Here again there is a delicate balance as to sex: which direction development shall take depends on the external conditions.⁸

Different Conditions as to Sex in different Organisms

There are many other conditions with respect to sex among different organisms. It will not be possible to deal with all these, but it will be worth while to enumerate some of the more important conditions.⁹

(a) Organisms with the two sexes in separate individuals, the sex being determined by differences in the chromosomes, as by the presence of one X or of two. It is mainly such organisms that have been dealt with in the foregoing pages. As we have seen, there are among these two groups, having diverse relations of chromosomes to sex. In Group I, the female has two X-chromosomes, the male but one; in Group II the reverse condition is found.

(b) Organisms having both sexes united in one individual (hermaphrodites). The same individual produces both ova and sperms. This condition exists in many organisms, as in common snails. The relations of this condition to chromosomes is not clear.

(c) Organisms in which the individuals are male during one period of their lives, female during another. Certain fish show this condition; it is indeed found in many animals.

(d) Organisms that are diverse as to sex in successive generations. Among these are to be distinguished several different types, as follows:

(1) Some organisms are hermaphrodites in one generation, but have separate sexes, male and female, in a later generation. Certain thread worms (Nematodes) show this condition.

(2) Some have no sex in one generation, reproducing without sperm and ova, but in the next generation have the two

OPERATION OF THE GENETIC SYSTEM

sexes, or are hermaphrodites. This is the condition found in plants.

(3) Some are exclusively female in certain generations, reproducing by parthenogenesis, the eggs not requiring fertilization. In a later generation there are both males and females. Many Rotifera are of this type.

The relation to chromosomes of these diverse conditions as to sex remains for the most part to be discovered. But the great variety of conditions found among organisms must be kept in mind, in order that the rôle of the chromosomes may not be misunderstood. They determine the sex through the fact that they act chemically; they determine it by altering the chemical conditions. Other things may alter the chemical conditions too, and then these also may determine sex.

In general, the relations of chromosomes to sex, brought out in the present chapter, demonstrate that the chromosomes affect development and characteristics through the fact that they influence the chemical materials and processes. Other conditions may likewise influence these processes, so that the effects of chromosomes may be modified or nullified by other conditions.

NOTES AND REFERENCES ON CHAPTER 3

1. Page 65. Important general works on sex determination are: E. Allen (Editor) (1932), *Sex and Internal Secretions*, 951 pages; F. Schrader (1928), *The Sex Chromosomes*, Berlin, 194 pages; R. B. Goldschmidt (1923), *The Mechanism and Physiology of Sex Determination*, 259 pages; E. Witschi (1929), 'Bestimmung und Vererbung des Geschlechts bei Tieren', *Handbuch der Vererbungs-wissenschaft*, Bd. II, Lieferung 10, 115 pages.

2. Page 67. For an exhaustive account of the chromosomes in man, with many figures, see H. M. Evans and O. Swezy (1929), 'The Chromosomes in Man, Sex and Somatic', *Memoirs of the University of California*, vol. 9, No. 1, 65 pages, 11 plates.

3. Page 68. See the following publications by C. B. Bridges: (1916) 'Non-disjunction as a Proof of the Chromosome Theory of Heredity', *Genetics*, vol. 1, pp. 1-52 and 107-163; (1922) 'The Origin of Variations in Sexual and Sex-limited Characters', *American Naturalist*, vol. 66, pp. 51-63; (1932) 'The Genetics of Sex in *Drosophila*': in Allen's *Sex and Internal Secretions*, pp. 55-93.

DIFFERENT CONDITIONS AS TO SEX

4. Page 81. F. R. Lillie (1917), 'The Free-Martin: A Study of the Action of Sex Hormones in the Foetal Life of Cattle', *Journal of Experimental Zoology*, vol. 23, pp. 371-451.

5. Page 84. T. H. Morgan (1909), 'A Biological and Cytological Study of Sex Determination in Phylloxerans and Aphids', *Journal of Experimental Zoology*, vol. 7, pp. 239-353.

6. Page 85. See T. H. Morgan and C. B. Bridges (1919), *The Origin of Gynandromorphs*, Carn. Inst. Publ. No. 278, pp. 1-122.

7. Page 86. See H. N. Gould (1917), 'Studies on Sex in the Hermaphrodite Mollusc *Crepidula plana*. II, Influence of Environment on Sex', *Journal of Experimental Zoology*, vol. 23, pp. 225-250.

8. Page 87. See F. Baltzer (1925), 'Untersuchungen über die Entwicklung und Geschlechtsbestimmung der *Bonellia*', *Pubblicazioni della Stazione Zoologica di Napoli*, vol. 6, pp. 225-286.

9. Page 87. Accounts of many of these different conditions as to sex will be found in Goldschmidt's *The Mechanism and Physiology of Sex Determination*, referred to in Note 1, above.

4

RELATION OF GENETIC SYSTEM TO CHARACTERISTICS

X-Chromosome as Type

In the preceding chapter it has been seen that differences in sex are produced by altering the chromosome combinations present in the fertilized egg, and this has brought to light some of the methods by which the chromosomes act on development and characteristics. We now examine other effects of altering chromosomes.

We shall have to examine the effects of altering all the different classes of chromosomes—the X-chromosome, the Y-chromosome, and the different autosomes. Each of these three groups (X, Y, and autosomes) gives rise, as we shall see, to a different type of inheritance. The simplest relations, from the experimental point of view, are presented by the X-chromosomes. We therefore deal first with these.

Effects on Characteristics produced by altering the X-Chromosomes. Sex-linked Inheritance

The X-chromosomes take such a course in passing from generation to generation that it is possible to follow the descendants of a particular X-chromosome (that present in the original male parent, for example), knowing in which individuals they are present, in which they are absent. Furthermore, in certain individuals (males, in organisms of Group I) there is but a single X-chromosome instead of a pair. These relations make it a relatively simple matter to discover the distinctive effects of a particular X-chromosome. The effects of X-chromosomes will therefore be dealt with somewhat

fully as a type of chromosomal action. Later the action of the other chromosomes will be taken up.

*Method of Inheritance of Characteristics resulting
from Modifications of X-Chromosomes*

The X-chromosomes, as we saw in Chapter 1, pass always from the father to his daughters, not to his sons. The sons get their X-chromosomes exclusively from the mother. These peculiarities make it relatively easy to discover characteristics of individuals that depend on the kind of X-chromosomes they contain. We saw in our introductory account of the discovery of the materials of heredity certain effects of altering X-chromosomes. Sometimes, as there set forth, an X-chromosome of one of the parents is defective in such a way as to cause an abnormality or defect in all the individuals that receive this X-chromosome or its descendants. Such an abnormality was bar-eye (Figs. 9 and 10). Characteristics of this sort, that are manifested in every individual that has the defective X, are called dominant characteristics.

It was further set forth that there are other characteristics which result from defective X-chromosomes, but which are manifested exclusively in individuals that carry only X's that are defective; if a normal X is present also, the characteristic does not appear. Such a characteristic was white eyes. Seemingly the defective X fails to produce certain required materials. But, if a normal X is present, it produces the materials, so that no defect results. Such characteristics, that are manifested only if a normal X is not present, are called recessive.

As we shall see in detail, many different characteristics are known that are thus due to defects or alterations in certain X-chromosomes. Such characteristics show very remarkable rules of inheritance. A number of such characteristics were known in man before their relation to chromosomes were discovered; their method of inheritance was extremely puzzling. It will be worth while to observe the rules of inheritance of such characters, as they appear when the relation to X-chromosomes is not brought out. In man there has long

GENETIC SYSTEM: RELATION TO CHARACTERISTICS

been known a defect called haemophilia, which follows this method of inheritance. It is due to a defective X-chromosome, and shows itself in the fact that the blood does not coagulate on exposure to the air, so that if wounded the defective individuals are likely to bleed to death. The defective X-chromosome fails to produce certain materials that are required for coagulation of the blood. But if a normal X is present in addition to the defective one, the necessary material is produced and the blood coagulates normally. Haemophilia is thus a recessive character. Colour-blindness is another recessive characteristic that is due to a defective X-chromosome.

The following are the rules of inheritance shown by such a recessive character resulting from a defective X-chromosome (see the diagram, Fig. 24).

(a) The individual affected by the abnormality is usually a male.

(b) When such an affected male mates with a normal female, none of the children are affected. It appears as if the defect were not inherited.

(c) But in the grandchildren the defect reappears; it has 'skipped a generation'.

(d) But not all the grandchildren have the defect. There is a peculiar distribution of the defect among them, as follows:

(1) None of the sons' children have the defect; nor does it reappear in any of their descendants. So far as the descendants through the sons are concerned, the defect has disappeared.

(2) But some of the daughters' children have the defect.

(3) None of the daughters' daughters have the defect.

(4) But some of the daughters' sons have it. On the average it turns out that about one-half of the daughters' sons have the defect.

(e) In later generations it continues *as a rule* in the way we have described, that is:

(1) Only males have the defect.

(2) It skips a generation, and reappears only in part of the *grandsons* through the *daughters*.

(3) It is thus inherited through normal females.

(4) But it is never inherited through normal males.

METHOD OF INHERITANCE OF CHARACTERISTICS

The above is the usual course of inheritance; it holds for the great majority of cases.

(f) But observers were perplexed by finding that in very rare cases all these rules are broken. The following were then observed (see Fig. 25):

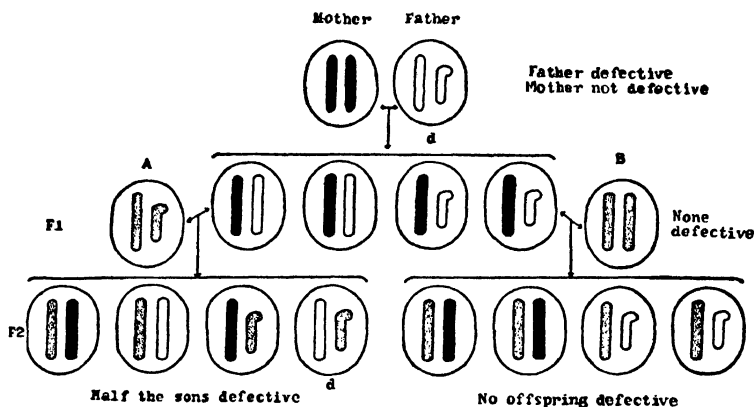


FIG. 24.—Diagram of the descent of a recessive defective X-chromosome, derived from the original male parent, in cases where there is no mating among relatives. Defective X represented in outline, normal X in solid black. The sons and daughters in F_1 , derived from the original mating, are conceived to mate with the unrelated individuals A and B, whose chromosomes are shown as stippled—the X-chromosomes of A and B not being defective. Defective individuals are marked d. In F_1 , none of the offspring are defective. In F_2 , half the daughters' sons are defective, while none of the sons' offspring (nor later descendants) are defective, since they lack entirely the defective X.

- (1) The individual affected is a male, as before.
- (2) He marries a normal female; and now some of the children are affected.
- (3) But not all the children are affected; on the average about one-half of all.
- (4) Those affected include both males and females, in equal number. Thus here we find that the rule that only males are affected does not hold; females also may have the defect.

(g) When now one of these rare defective females is mated with a normal male:

GENETIC SYSTEM: RELATION TO CHARACTERISTICS

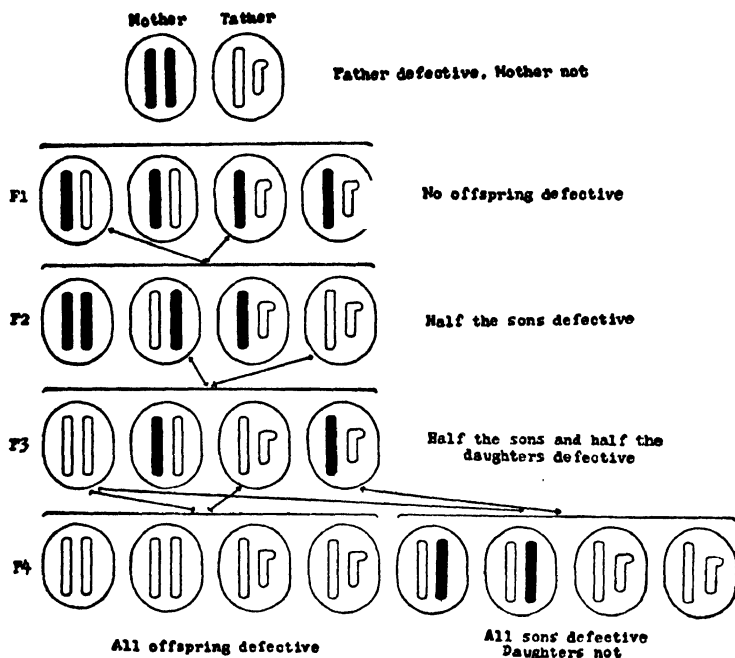


FIG. 25.—Diagram to illustrate the descent for successive generations of a defective X-chromosome derived from the original male parent, when there is inbreeding among the descendants, with the various types of results produced. The defective X-chromosome is represented in outline, while the normal X-chromosomes, derived from the mother, are represented in solid black. (The Y-chromosome, found in males only, is represented as smaller and hooked.) The horizontal rows of outlines show the chromosomal conditions in the individuals of successive generations (F₁ to F₄) derived from the two parents at the top. Females (with two X-chromosomes) are at the left; males (with X and Y) are at the right. The arrows indicate the parentage of the successive generations. The defective X produces a recessive personal defect, so that individuals containing only the defective X (with or without Y) are personally defective. All individuals containing a normal X (black) are normal.

- (1) All the sons produced are affected.
- (2) None of the daughters are affected.

METHOD OF INHERITANCE OF CHARACTERISTICS

Thus 'the sons inherit from their mothers, the daughters from their fathers', in such a case.

One further important fact was observed:

(*h*) If the mother and father are both affected, then all children are affected, including daughters as well as sons.

Imagine trying to get intelligible rules of inheritance from such a set of seemingly contradictory observations! Even the rules commonly followed seem arbitrary and incomprehensible. And at times they are all broken; sometimes one result is produced, sometimes another.

But when it was discovered that such defects are due to a defective X-chromosome, and that they appear wherever the defective X-chromosome has no normal one with it, all this was at once cleared up and became intelligible. This is revealed at once when we place in the diagram the X-chromosomes of the individuals, marking in a special way the X-chromosome of the individual originally affected (see Figs. 24 and 25), and in the same way all the X-chromosomes derived from that chromosome. Every individual that contains only the defective X is itself defective, whether male or female. Every individual that contains in addition a normal X is without the defect. Such defects usually appear in males only, because males have only one X-chromosome; and if that is defective, the individual is defective. Females, on the other hand, have two X-chromosomes, and as normal X's are more common than defective ones, usually any female that has a defective one has a normal one also, and is therefore not personally defective.

But rarely it happens by chance that a female gets two defective X-chromosomes; then, having no other, she is personally defective. And in that case, since she always gives one of her X's to her sons and they have no other, her sons are all defective.

Indeed, when we recognize that such a characteristic as haemophilia or colour-blindness is due to a defect in certain X-chromosomes, but is not manifested if a normal X-chromosome is present, we discover that all the results enumerated above, and illustrated in the diagram of Fig. 25, are inevitable.

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Many other recessive characteristics, as we shall see, are due to defects or modifications of X-chromosomes. Such characters are distributed to the offspring in the way illustrated above; they all follow the same rules of inheritance. They follow the defective X wherever it goes, being manifested whenever the defective X is the only kind of X that is present. Such characters, since they are commoner in males, are commonly called sex-linked characteristics.

In the case of certain serious defects, these rules are modified by the fact that individuals with two defective X's (females) cannot live and develop. Haemophilia, for example, is not certainly known to occur in females. Any female that gets two X's defective in this way simply does not live. Colour-blindness, however, illustrates well all the rules set forth above, and the same is true for many such defects in animals.

Abnormal Distribution of X-Chromosomes

What will happen if the X-chromosomes by accident become irregularly distributed? We have seen in Chapter 3 that sometimes the X-chromosomes are indeed irregularly distributed. Will the sex-linked characteristics continue to follow them; will the defective characteristics show the same irregular distribution as do the X's?

Such cases in great number have been fully observed. It is found that the sex-linked characteristics do indeed follow the X-chromosomes wherever they go. This proves conclusively (if there were any possible doubt in view of the extraordinary course normally followed by such characters) that it is indeed the X-chromosomes on which the characters depend. The matter is one of importance and interest, so that it will be worth while to examine carefully certain typical cases of the result of irregular distribution of X-chromosomes.

Normal Distributions (Fig. 26, A).—Sometimes the body of *Drosophila* is yellow instead of the normal grey; this is a recessive character due to a defect in the X-chromosomes. Suppose that we mate together a female that has a yellow

ABNORMAL DISTRIBUTION OF X-CHROMOSOMES

body and a male that has the normal grey colour. The female has two modified X-chromosomes, which we may represent by XX . The male has its X unmodified; we may represent its cells as XY . Normally in forming the germ cells, the two X's of the female separate into different germ cells, and all the ova receive one of the modified X's. The normal male produces germ cells of two classes, X and Y. When the germ cell X from the female unites with Y from the male, sons are produced, with the constitution XY ; while X from the female with X from the father gives daughters XX . Since the yellow colour dependent on X is recessive, the daughters XX have the normal grey colour, like the father. But the sons XY have only one X, and as this is the defective one, from the mother, the sons are yellow, like the mother. The normal result of such a mating therefore is that all the sons are recessive like the mother, all the daughters dominant, normal, like the father. This is what occurs when the X-chromosomes are distributed to the germ cells in the usual way.

Abnormal Distribution (Fig. 26, B).—Sometimes, as seen on previous pages, in forming germ cells both X's of the female go together to a single ovum, while other ova receive no X (see Fig. 20). In a race discovered by L. V. Morgan¹ the two X-chromosomes in the female were partly united, so that they almost invariably thus go together to one ovum, leaving other ova without an X. In this race the X-chromosomes were so modified as to produce the recessive yellow colour described in the preceding paragraph. We therefore have an opportunity to determine the course of inheritance of the yellow and the grey colour when the X-chromosomes are thus abnormally distributed.

Represent as before the X-chromosomes that produce the yellow colour by X. Thus one set of ova receive XX , while another set receive no X. (See the diagram, Fig. 26, B). When the germ cells XX united with the germ cells Y from the normal father, there were produced daughters XXY , in which both X's came from the mother, and *these daughters were yellow* like the mother (since no normal X was present). Sons were produced by the union of ova that contained no X with

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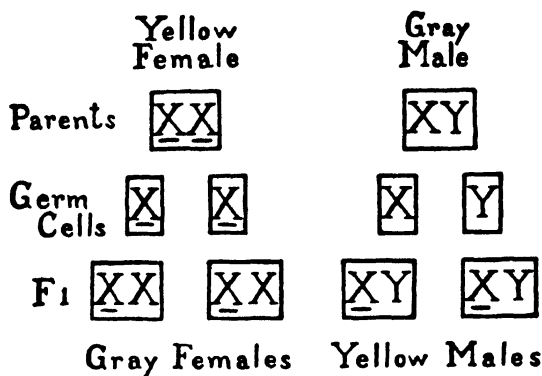


FIGURE A

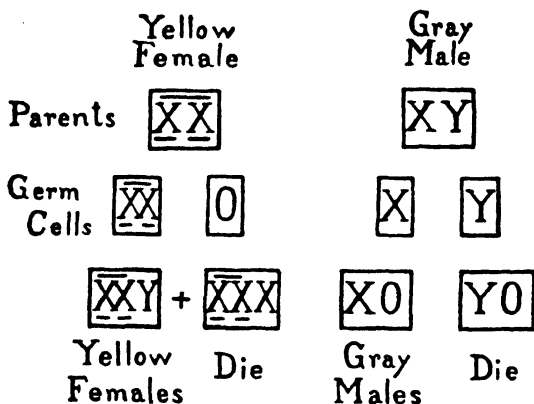


FIGURE B

FIG. 26, A and B.—Diagrams to illustrate inheritance through the X-chromosomes, in cases in which the distribution of the X's is normal (Fig. 26A), and in those in which the two X's of the female are united, so that they go together to the same germ cell (Fig. 26B). The underlined X's are recessive, producing yellow; those not underlined are dominant, producing grey. The two X's having a bar above them (in B) are the united X's, both going to the same germ cell, and leaving other germ cells (O) without X or Y.

Fig. 26, A, normal distribution: sons like the mother, daughters like the father. Fig. 26, B, abnormal distribution: sons like the father, daughters like the mother. See text.

ABNORMAL DISTRIBUTION OF X-CHROMOSOMES

sperms that carried X; this gave sons XO, with their single X from the normal father, instead of from the mother, as is usually the case. And *such sons had the normal grey body colour of the father*, instead of the yellow body colour of the mother, as happens normally.

Thus with a change in the distribution of the X's there is a corresponding change in the method of inheritance. If the sons receive their X from the recessive mother, as in the normal cases, they are recessive like the mother. But when, through non-disjunction, the sons receive a dominant X from the father, they are dominant like the father. Similarly, in the normal case the daughters receive a dominant X from the father and are therefore dominant like the father. But in cases of non-disjunction the daughters receive both their X's from the recessive mother, and are therefore recessive like the mother. In sum, when the X's are normally distributed, such matings give 'criss-cross inheritance'; sons like the mother, daughters like the father. But when the X's are not so distributed, there is no criss-cross inheritance; sons are like the father, daughters like the mother. The dominant and recessive characters follow the respective X-chromosomes, whether these are distributed normally or abnormally.

Such experiments have been repeated many times, and with other sex-linked characters. Always the characteristics follow the distribution of the X-chromosomes, however these are distributed.

It may be concluded with certainty that it is the presence of X-chromosomes of a modified type that causes the appearance of the particular sex-linked characters that are manifested. The rules of distribution of sex-linked characters are the rules of distribution of the X-chromosomes.

Dominance and Recessiveness in Sex-linked Characters

As we have seen, and shall see further, many defective conditions are due to defects in certain X-chromosomes. These follow from generation to generation the distribution of these X-chromosomes. Most of these bodily defects are

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manifested only in individuals in which the defective X-chromosomes are the only kind present; that is, these defects are recessive.

But it is important to observe that in such cases the normal condition of the organism likewise follows the distribution of certain X-chromosomes. Haemophilia follows certain X-chromosomes. But in the same matings in which this occurs, the healthy condition of the blood follows certain other X-chromosomes. If a defective mother is mated with a normal father, the sons are defective because they receive only the mother's defective X-chromosomes. But in the same way the daughters are normal because they receive the father's normal X-chromosomes. In the normal individuals the X-chromosome plays a part, just as it does in the defective individuals. In the normal individuals it is healthy and supplies what is required for normal development, while in the defective individuals it fails to supply what is required.

In the case of most defects this normal condition is dominant over the recessive condition; that is, when both are present, the normal chromosome is the one that prevails in its effect on the individual. There are defective characters, however, in which the defective condition is dominant or partly dominant. In these cases, when a defective X and a normal one are present together, the defective one produces its effect, as in the case of bar-eye, described in Chapter 1. In many such cases the defect is less marked when a normal chromosome is present as well as a defective one; then the defective condition is said to be partly dominant.

Thus whenever an individual bearing defective X-chromosomes is mated with a normal individual, we have both dominant and recessive characters, the course of which may be followed in the later generations—the dominant character being commonly the normal or usual condition. How this works out is shown in our next paragraphs.

Tests for Sex-linked Inheritance.—By observing the distribution of the dominant and recessive characters among the offspring of certain matings, a test for determining whether given characters depend on the X-chromosomes is supplied.

TESTS FOR SEX-LINKED INHERITANCE

The test consists in making what are called reciprocal crosses: (1) On the one hand mate a dominant female with a recessive male; (2) also mate a recessive female with a dominant male.

Represent a dominant X-chromosome by a capital X, a recessive X-chromosome by a lower-case letter x . In the group of organisms with which we have been dealing, the female has two X-chromosomes, the male but one. The daughters receive an X from each parent, the sons an X from the mother only.

A dominant female will be represented by XX, a recessive male by xo ; similarly a recessive female is xx , a dominant male is XO. The two matings and their results will then be represented as follows:

(1)	XX	by xo gives	X x	+	XO
	Dom. Mother	Rec. Father	Dom. Daughters		Dom. Sons
(2)	xx	by XO gives	X x	+	xo
	Rec. Mother	Dom. Father	Dom. Daughters		Rec. Sons

Thus when the mother is dominant, the father recessive, all the children are dominant, like the mother. When the father is dominant, the mother recessive, the daughters are dominant like the father, the sons recessive like the mother; this is called 'criss-cross inheritance'.

Whenever reciprocal crosses give these results, it is certain that the two diverse characteristics (dominant and recessive) result from differences in the X-chromosomes of the two parents. 'Criss-cross inheritance' is particularly useful in showing at once that we are dealing with sex-linked inheritance. In every case where such results are produced, further tests show that the two characteristics follow in later generations the two different kinds of X-chromosomes wherever they go. It is mainly by the use of these tests that the many different characteristics dependent on diversities in X-chromosomes have been discovered.

Sex-linked Inheritance in Group II.—Sex-linked inheritance as we have just described it was originally discovered in animals belonging to Group I, in which the females have two

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X-chromosomes, the males but one (with or without a Y-chromosome).

But when the tests we have just described were applied to birds and to certain other animals, it was discovered that there is a second group (Group II) in which it is the male that has two X-chromosomes, the female but one. In the common fowl, reciprocal crosses were made between 'barred' fowls (Plymouth Rock) and black fowls (Langshan). Here the 'barred' condition was found to be dominant. The results were:

(1) Barred father by black mother = Barred sons + barred daughters.

(2) Black father by barred mother = Barred sons + black daughters.

Here the second mating gives 'criss-cross inheritance', showing that we are dealing with sex-linked characters dependent on differences between the X-chromosomes of the parents. But, in the first mating above, all the offspring are like the father instead of like the mother, which latter was the case in the matings on the previous pages. The father in this case has the dominant characteristic (barred), and all the offspring are dominant like the father instead of like the mother. When the mother is dominant ('barred') the result in the fowls is criss-cross inheritance; while, in the cases before described, criss-cross inheritance occurs when it is the father that is dominant. In fact, in the birds, the males and females simply exchange rôles, as compared with their rôles in the organisms of Group I. This appears clearly from the following comparison of results in the two cases:

<i>Parents</i>		<i>Offspring</i>
(1) Group I. Dom. Mother, Rec. Father	}	All Offspring dominant
Group II. Dom. Father, Rec. Mother		
Chromosomes — XX	xo	Xx — XO
(2) Group I. Dom. Father, Rec. Mother:—Dom. Daughters, Rec. Sons		
Group II. Dom. Mother, Rec. Father:— Dom. Sons, Rec. Daughters		
Chromosomes — XO	xx	Xx — xo

Since the rôles of males and females are interchanged in the two groups, their chromosomal conditions must also be

WHAT CHROMOSOMES DEPEND UPON ALTERATIONS?

interchanged; that is, since in Group I the female has two X's, and in Group II the male plays the same rôle as the female of Group I, the male of Group II must have two X's, the female but one. The chromosomal conditions in the two groups are shown in the above tabulation, X signifying dominant, while x signifies recessive, and o signifies the lack of X (whether Y is present or not). Careful examination shows that this is the only way in which the results in Group II can be produced.

It was in the way illustrated above that the existence of Group II was discovered. Birds and certain moths show inheritance of the kind typical for Group II. In both these it has since been found under the microscope that the males have indeed one more chromosome than the females.

What kinds of Characteristics depend upon Alterations of the X-Chromosomes? The Rôle of the X-Chromosomes in Development

A great many characteristics, of various kinds, have been found to be the result of modifications of particular X-chromosomes, and thus to follow in later generations the distribution of the descendants of those chromosomes. Examination of a number of these is desirable, both for their own importance and for the light they throw on the functions of the X-chromosomes.

In man,² the following characteristics, among others, dependent on diverse types of X-chromosomes, are known from the fact that they show typical sex-linked inheritance.

Haemophilia.—Lack of coagulability in the blood. This results from a serious defect in certain X-chromosomes. The existence of defective X-chromosomes having this result shows that the normal X-chromosomes play a part in supplying something necessary for producing normal blood that coagulates properly.

Colour Blindness. The fact that defectiveness in X-chromosomes causes colour blindness shows that the normal X's play a rôle in producing the normally functioning eyes.

GENETIC SYSTEM: RELATION TO CHARACTERISTICS

Night Blindness.—Inability to see in a poor light.

Near-Sightedness of certain types.

Progressive atrophy of the muscles (Gower's disease).—The fact that defects in X-chromosomes have this effect shows that the normal X's play a rôle in the normal functioning of the nerves and muscles.

A considerable number of other sex-linked characters are known in man. But man is a very unfavourable organism for the study of inheritance. Yet even the little that is known of sex-linked inheritance in man shows that the X-chromosome plays a rôle in many diverse bodily functions. For a more complete idea of its rôle, some organism that can be bred experimentally must be examined. For this purpose the fruit-fly, *Drosophila melanogaster*, is the best organism to select, since it has been studied more extensively than any other.

In the fruit-fly we find peculiarities of the following types that are dependent on alterations in particular X-chromosomes:

Many different eye colours. The normal eye colour in this organism is a certain shade of red. Defects in different X-chromosomes result in producing, in the individuals that bear these defective chromosomes, many different shades of red, varying from deep red to a very light red, and thence to 'buff', 'ivory', and 'white'. More than a dozen different types of eye colour are known to result from modifications of the X-chromosome. It is clear that the normal X-chromosome plays an important rôle in producing the normal eye colour.

Structural peculiarities of the eye, such as 'bar-eye', described in our introductory chapter, 'facet eye', 'furrowed eye', and the like, are known to result from modifications of the normal X-chromosome.

Wing modifications.—Many different conditions of the wings are known that depend upon diversities among X-chromosomes borne by different individuals. These affect all sorts of features of the wings: size, form, venation, function. The normal X-chromosome obviously plays an important rôle in the full and normal development of the wings.

RÔLE OF X-CHROMOSOMES IN DEVELOPMENT

Body colours and markings.—Modifications of the X-chromosomes produce the body colours yellow, sable, tan, chrome, lemon, green, and the like, in place of the normal grey. Other changes in X alter the distribution of pigment on the body, giving the characters '*dot*', and the like.

Body structure.—A defect in X produces irregularities in the abdomen, known as 'abnormal abdomen'.

Legs.—A defect in X-chromosomes causes abnormal development of the legs; some of them are wholly or partly reduplicated, so that the total number of legs is increased.

Bristles.—Modifications in X-chromosomes result in various different changes in the bristles that are scattered over the body.

Many physiological conditions and functions likewise depend upon the X-chromosomes, since they are changed when these chromosomes are modified. Among these are the following:

Positive reaction to light. *Drosophila* with normal X-chromosomes fly toward a source of light. Those having defective X-chromosomes of the kind that produce a tan-coloured body do not fly toward a source of light.

Weakness and short life. Most of the defective X-chromosomes that cause structural or other changes in the body (different eye colours, wing forms, and the like) produce likewise weakness and short life. The individuals bearing them are less resistant to bad conditions, and live for a shorter time than the individuals that bear the normal X-chromosomes.

Life and death. Some X-chromosomes have defects that are so severe that the individuals bearing them will not live and develop, unless there is present also a normal X-chromosome. Such defects are known as lethals. The presence of such lethal defects in the X-chromosome has the result that males bearing them die, since they have but one X; while females usually live, since they have an additional X that is often normal. If a mother that has one lethal X and one normal one is mated to a father that has a normal X, the result is that half of the sons which receive the mother's defective X fail to develop, while the other half of the sons,

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receiving the mother's normal X, live and develop. All the daughters live, since they all receive a normal X-chromosome from the father. The consequence is that in such families there are twice as many daughters as there are sons. In families of 100 to 200, as occur in *Drosophila*, this is very striking.

X-chromosomes are known to play in other organisms rôles similar to those mentioned above for *Drosophila*, although in no other organism has the matter been so fully studied.

We may summarize what has been brought out above in the following statements:

1. Many defects that appear in individuals are the result of defects in the X-chromosomes that they bear.
2. Some of these defects are dominant; they are manifested in all individuals in which the defective X is present.
3. But most such defects are recessive; they are manifested only in individuals in which the defective X is the only kind present.
4. When both a normal X and a defective X are present, in most cases the normal X performs the required functions, so that the individual is not defective.
5. Since the female has two X-chromosomes, while the male has but one, such defects are more frequently manifested in the males. Usually one of the X's present in the female is without the defect, so that she is not defective. But when the male carries a defective X-chromosome, the defect is manifested.
6. It is thus advantageous, so far as the occurrence of defects is concerned, to have two X-chromosomes rather than one.
7. This gives the female a considerable advantage over the male in these respects. There are many different types of defects due to defective X-chromosomes; almost all of them are more common in males than in females. Some of these defects seriously injure the health, or even result in death, if the defective X is the only kind that is present. It is well known that, in general, the death rate is higher in males than in females; this is probably due to the fact that males have but one X-chromosome.

RÔLE OF X-CHROMOSOMES IN DEVELOPMENT

8. Among the different individuals of a species are scattered a great number of different types of X-chromosomes having different effects on development. Many of the diverse X-chromosomes are distinctly defective, causing personal defects in the individuals that bear them. Others are not defective.

9. Defects or modifications in X-chromosomes affect in different cases all parts and functions of the organism.

The Rôle of the X-Chromosomes in Development

What do the facts brought out in the preceding sections show as to the physiological functions of the X-chromosomes; as to their rôle in development?

For every kind of effect resulting from defects or modifications in the X-chromosomes, there is a corresponding (opposed or diverse) action of normal or unmodified X-chromosomes. Since defective X-chromosomes of a certain type produce in *Drosophila* short, ill-developed wings, it follows that the normal X-chromosomes act on the development in such a way as to give long, well-developed wings. For if we substitute the normal X for the defective one, this causes the normal well-developed wings to be produced. Similar reasoning applies to all the defective conditions that result from defective X's; the normal X's act in such a way as to produce the corresponding normal conditions.

It follows therefore that the normal X-chromosomes play a rôle in the production of eye colour and structure, body colour and structure, in the development of the legs, the wings, the bristles, in producing normal health, resistance and vigour, and in various physiological processes. We know, further, that they play a most important part in determining sex, with all that this includes of structural and physiological influence (Chapter 3).

Clearly therefore the X-chromosomes play a most important part in development. Their action is not limited to any single part of the body, nor to any single class of functions. They enter into the processes of development in such a way

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as to influence all parts of the body, all functions of the body. They begin to influence development very early, as was seen in considering the development of sex. And they play important rôles in such relatively late processes as the production of eye colours. It can hardly be doubted that they enter into the developmental activities from practically the beginning, influencing all the later processes that occur.

NOTES AND REFERENCES ON CHAPTER 4

1. Page 97. See L. V. Morgan (1922), 'Non-criss-cross Inheritance in *Drosophila melanogaster*', *Biological Bulletin*, vol. 42, pp. 267-273.
2. Page 103. For inheritance of characteristics in man, see R. R. Gates (1929), *Heredity in Man*, 385 pages, London; also E. Baur, E. Fischer and F. Lenz (1931), *Human Heredity*, 734 pages, New York.

5

RELATION OF GENETIC SYSTEM TO CHARACTERISTICS

Autosomes and Y-Chromosomes

In the two preceding chapters the X-chromosomes have been dealt with because of the great advantages they offer for experimental study. It was seen that they affect development in many ways, and that in a given species there are many different types of X-chromosomes in the different individuals, causing them to show different characteristics, structural and physiological.

Is the X-chromosome typical in these relations? Shall we find similar effects in the other chromosomes?

In addition to the X-chromosomes, there are the autosomes, which are present as a rule as several or many pairs. In man there are 23 pairs of autosomes (Fig. 19): in *Drosophila* there are three pairs (Fig. 7). There is, further, in many species the single Y-chromosome. The autosomes and the Y-chromosome are distributed from parent to offspring in characteristic ways, differing from the distribution of X-chromosomes. If they affect characteristics, these differences should appear in a different system of inheritance. We shall examine first the autosomes.

The Autosomes: Typical Mendelian Inheritance

We have already seen that the autosomes play a rôle in development, in the fact that they help to determine the sex of the developing individual. In *Drosophila*, if the number of sets of autosomes, in relation to the number of X's, is changed, this changes the sex (see Chapter 3).

Do autosomes also affect other characteristics? Do the

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different pairs of autosomes have different functions? Are there diverse types of autosomes, with different effects, in different individuals of a species, as is the case in relation to the X-chromosomes? Are there dominant and recessive effects of autosomes, as there are of X?

If dominant and recessive characteristics depend on autosomes, then these characteristics must follow the distribution of the autosomes from parents to offspring, as the characteristics dependent on X follow its distribution. We must then examine the method of distribution of the autosomes, to see whether there are characteristics that show this method.

Method of Distribution of the Autosomes.—The distribution of the autosomes from parents to offspring is much simpler than that of the X-chromosomes. The main facts are as follows:

1. The autosomes are in pairs in all individuals (Figs. 3, 6, 7). There are no individuals with unpaired autosomes, like the male of some organisms with relation to X.

2. Thus the two sexes are alike as to their autosomes.

3. In forming germ cells, one member of each pair of autosomes goes to each germ cell (Fig. 4). The sperms and the ova are alike with respect to the autosomes.

Thus the fundamental rule with relation to the autosomes is that *each germ cell carries one member of each pair of autosomes*.

4. By union of two germ cells the pairs of autosomes are restored (Fig. 5).

5. Thus each one of the offspring carries in each pair of its autosomes one autosome from each parent.

Now consider a single pair of autosomes, such as the pair marked AA in Fig. 27. Suppose that in different individuals the members of this pair of autosomes produce different effects, as we have seen to be the case with the X-chromosomes of different individuals. And suppose that, as in the case of X, one of these effects is dominant, the other recessive. How would such characteristics be inherited?

This question must be examined with care. For this purpose we may take as an example the different colours found in different varieties of peas, used in the classic experiments of Mendel.¹ The yellow seed colour of a certain variety is

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dominant, and results from the constitution of the autosomes of a certain pair. The green seed colour of another variety is recessive, owing to a different constitution of the autosomes of that same pair.

Call the two autosomes of that pair in the dominant yellow

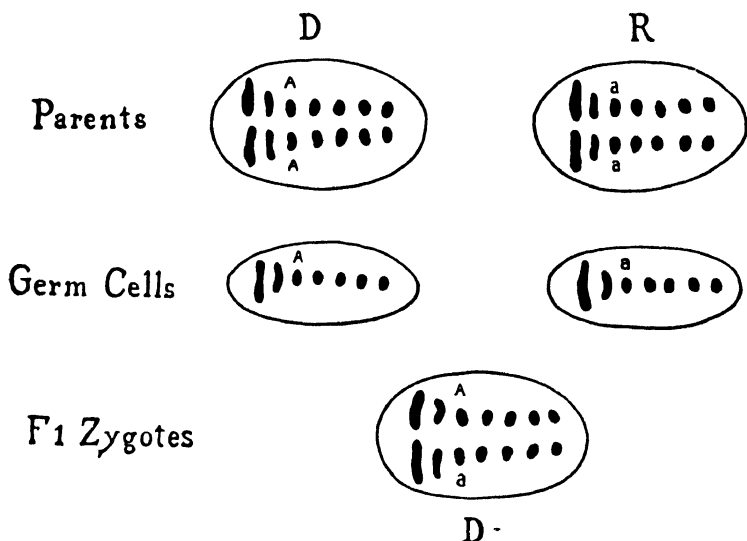


FIG. 27.—Diagram to illustrate the results of mating dominant and recessive parents (D and R), differing in a single pair of autosomes, AA and aa. The offspring F_1 are all heterozygote dominants Aa.

race by the capital letters AA, while the two autosomes that give rise to the recessive green colour in the other race may be called aa. The dominant parent may be designated D, the recessive parent R, as in Fig. 27.

When these two parents produce germ cells, each germ cell receives, of course, one chromosome for the pair. The germ cells from the dominant parent D have the autosome A, those from the recessive parent R have the autosome a (Fig. 27).

The germ cells A, from parent D, unite each with a germ cell a from parent R (Fig. 27), giving offspring (zygotes) containing both A and a. These first generation offspring are commonly designated F_1 (first filial generation), as in Fig. 27.

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And since the characteristic carried by the autosome *A* is dominant, all these *F*₁ offspring manifest the dominant characteristic *D* (yellow, in case yellow-seeded peas are crossed with green-seeded peas).

Next observe the result of mating together two of these individuals *Aa*, of the *F*₁ generation, giving the *F*₂ (second filial generation), as in Fig. 28.

Each parent *Aa* gives, according to the general rule, two kinds of germ cells, one kind carrying the dominant autosome *A*, the other the recessive autosome *a*. Each kind of germ cell from one parent unites with each kind from the other. That is, half the *A* germ cells from one parent unite with *A* germ cells from the other parent, half with *a* germ cells from the other parent; and the same is true for the *a* germ cells from the first parent. This gives in equal proportions *F*₂ offspring (zygotes) as follows (Fig. 28):

$$AA + Aa + aA + aa$$

But as the two combinations *Aa* and *aA* contain the same chromosomes, the proportions may be written

$$AA + 2Aa + aa$$

The individuals of the constitution *AA* and *Aa* contain the dominant chromosome *A*; therefore they manifest the dominant characteristic, *D*. The individuals *aa*, having only the recessive chromosome *a*, manifest the recessive characteristic, *R*. Thus in this *F*₂ generation, so far as manifested characters are concerned, the proportion of offspring are—

3 Dominant to 1 Recessive

Thus if dominant and recessive characteristics depend on the two members of a pair of autosomes, when a dominant individual *AA* is mated with a recessive individual *aa* the general result is bound to be that the immediate offspring (*F*₁) all manifest the dominant characteristic, while in the *F*₂ generation (produced by mating two individuals from *F*₁) there will be three times as many dominant individuals as there are recessives.

Now, this is the result that was discovered by Mendel in 1866; it formed the foundation for the working out of Men-

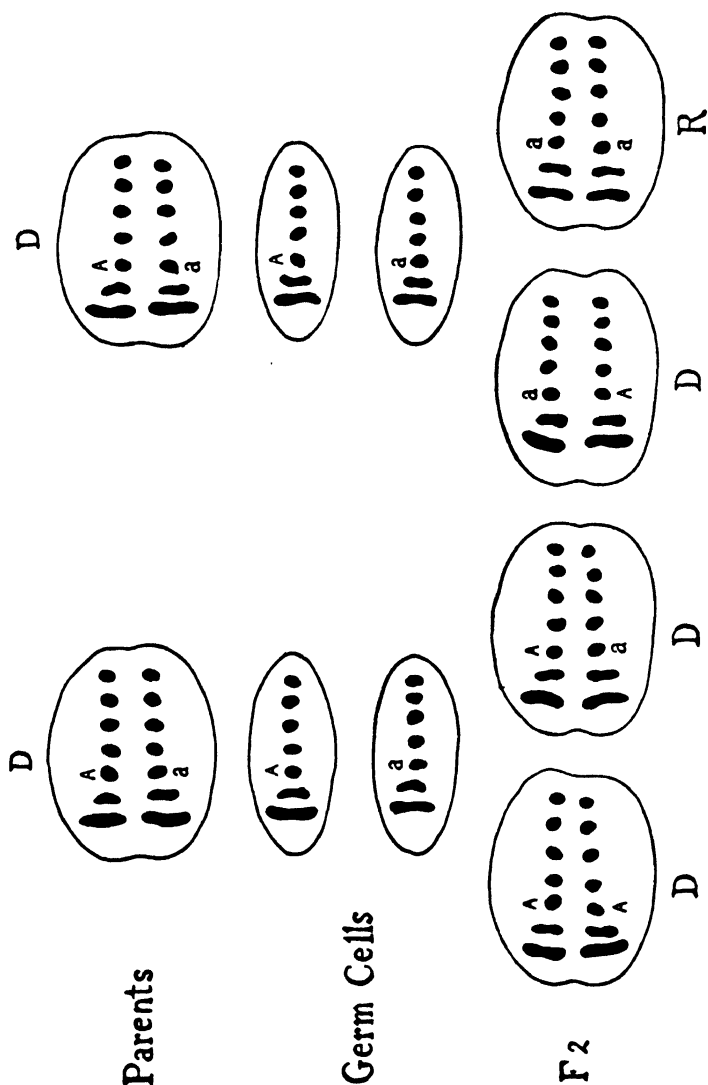


FIG. 28.—Diagram to illustrate the results of mating two *F*₁ heterozygotes *Aa*, to produce generation *F*₂. *D*, dominant; *R*, recessive.

delian heredity. The proportion 3*D* to 1*R* in the *F*₂ generation is commonly known as 'the Mendelian ratio'; it is one of the most characteristic proportions in this type of inheritance.

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Mendel discovered that there are many different characteristics that yield this 3 to 1 ratio. If yellow and green peas are crossed, in the F₂ generation there are 3 yellows to 1 green; if round peas and wrinkled peas are crossed, in F₂ there are 3 round to 1 wrinkled; and so for many other characteristics in the pea plants with which Mendel worked.

And since the time of Mendel these same ratios have been found for thousands of different characteristics, in great numbers of different organisms, from the pea plant and *Drosophila* to man. The fact that inheritance gives these ratios is commonly spoken of as Mendel's law, and the type of inheritance which it exemplifies is spoken of as Mendelian inheritance. The type that gives in the F₂ generation 3D to 1R is the commonest method of inheritance, much commoner than the sex-linked method, in which the characteristics depend on differences in the X-chromosomes. This is obviously because autosomes are more numerous than X-chromosomes.

We find then that inheritance according to Mendel's law takes place exactly as it would if the characteristics concerned depended on the two members of a pair of autosomes. As will be shown later, it can be proved experimentally that such characteristics do indeed depend upon autosomes.

Thus the rules of Mendelism are the rules of distribution of the two members of a pair of autosomes, one having a recessive effect, the other a dominant effect. Mendelian heredity is heredity of characteristics that depend on differences in autosomes.

Mendel did not know of the relation of the characteristics to the chromosomes. He discovered, however, certain other important facts about this type of heredity, facts which have become clearly explicable since it has been learned that this type depends on differences in autosomes. These facts must be examined.

For this purpose it will be convenient first to define certain terms which are universally employed in dealing with inheritance.

By the union of two germ cells or gametes, as A and a, there is produced a zygote. If the two germ cells are alike

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with respect to the chromosomes or characteristics that they carry, the zygote so produced is spoken of as a *homozygote*; thus AA and aa are homozygotes. If the two germ cells that unite to form a zygote are unlike, as A and a, the zygote so produced is called a *heterozygote*, as Aa.

The two corresponding characters, one dominant, the other recessive, that are produced by the two differing members of a pair of chromosomes are spoken of as alternative characters, or *alleles*, or *allelomorphs*. Any given individual manifests one or the other of the two alternatives, not both. For the alternative characters we shall employ henceforth the term alleles.

The characteristic manifested by a zygote is its *phaenotype*, while its actual constitution is its *genotype*. Thus, two zygotes AA and Aa both manifest the dominant character; the dominant character is the phaenotype, or the individuals are said to be phaenotypically dominant. But they are diverse in genotype; one is AA, the other Aa. In the case of a homozygote AA or aa, the phaenotype and genotype may be held to coincide.

Mendel crossed yellow peas with green peas, and found, as before stated, that in the F₁ generation all the peas were yellow, so that yellow is the dominant allelomorph. In the F₂ there were three times as many yellows as greens. The actual number of seeds in the F₂ generation was in his experiments 8023, of which 6022 were yellow while 2001 were green, so that the ratio of dominants to recessives was, accurately expressed, 3.01 to 1.

Mendel found that if he bred further the individuals of the F₂ generation, some of these gave different results from others. In the pea plant it is possible to allow each plant to fertilize itself, so that both kinds of germ cells come from the same parent. When this was done with the individuals of the F₂ generation, the following results were observed:

The green plants (recessive) gave only recessive green offspring (they 'bred true').

Of the yellow plants (dominant), one-third gave only yellow offspring (they 'bred true'), while two-thirds of them

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gave both yellow and green offspring, in the proportion of 3 yellows to 1 green.

The reason for this is clear when we consider the chromosomes on which the characters depend. If *A* represents the chromosome (autosome) that gives the dominant yellow colour, while *a* represents the chromosome that gives the recessive green, the original parents were *AA* and *aa*, the *F*₁ generation were all *Aa*, while the *F*₂ generation showed the proportions

$$AA + 2Aa + aa$$

The recessive individuals *aa* are homozygotes; their two chromosomes are alike, being *aa*. When germ cells are produced by these homozygotic individuals, all these germ cells must contain the chromosome *a*, and when two of these unite in self-fertilization, of course they produce in all cases again individuals *aa*. These are, of course, recessives (green), like their parents; that is, the green parents *aa* 'breed true'.

Similarly the dominant yellows, *AA* (constituting one-third of all the dominants), are homozygotes. Their germ cells all contain the chromosome *A*, and the offspring produced by union of such germ cells, in self-fertilization, are all *AA*, and so dominant yellow like the parents. One-third of all the dominants thus breed true.

But the individuals *Aa* are heterozygotic; that is, they have two kinds of chromosomes, *A* and *a*, in the pair. Thus they produce two kinds of germ cells, *A* and *a*, in equal numbers. And when these germ cells unite, they necessarily give, as we saw on an earlier page, offspring of three kinds, in the proportions

$$AA + 2Aa + aa$$

Of these, *AA* and *2Aa* will be dominants (yellow), while *aa* will be recessive (green).

Thus the homozygotes *aa* and *AA* breed true, while the heterozygotes, *Aa*, do not.

Furthermore, as Mendel discovered, if the heterozygotes *Aa* are mated with the recessive homozygotes *aa*, they give two kinds of offspring, *Aa* and *aa*; half (*Aa*) being dominant,

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the other half (aa) being recessive. If the heterozygotes Aa are mated with the dominant homozygotes AA, the offspring AA and Aa are all dominant, though half (AA) are homozygotes, the other half (Aa) heterozygotes.

All these results are typical for the descendants of two parents different in a single pair of chromosomes, one pair being dominant, the other recessive. For reference it will be well to make a table of these results, characteristic for Mendelian inheritance:

TABLE I, FOR THE RESULTS OF MENDELIAN INHERITANCE

Parents: AA and aa; both homozygotic.

F₁: Aa; all alike, dominant heterozygotes.

F₂: AA + 2Aa + aa. Three-fourths of the individuals dominant, one-fourth recessive. Half the individuals homozygotes (AA and aa), the other half heterozygotes (2Aa).

Each type of homozygote bred by itself produces offspring like itself.

The heterozygotes Aa, when bred by themselves, produce again offspring

$$AA + 2Aa + aa$$

Aa mated with aa yields again Aa + aa

Aa mated with AA yields again Aa + AA

All of these results are found to hold true for thousands of different characteristics. We may therefore summarize the situation in the following general propositions:

1. When two different individuals are crossed, in many cases the differences between them follow the same method of distribution as do the two members of a pair of autosomes—one being dominant, the other recessive.

2. This distribution is what is known as typical Mendelian heredity.

3. The two sexes do not differ in these respects. Each sex has the same proportion of dominants and recessives.

4. The rules of Mendelian inheritance are essentially the rules of distribution of the members of pairs of autosomes.

Characteristics that depend on two or more pairs of autosomes.—We have thus far followed the distribution of characteristics that depend on differences in a single pair of

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autosomes. But most organisms have several or many pairs of autosomes: the fruit-fly has three pairs, man has twenty-three. Do some characteristics depend on differences in one pair of autosomes, others on differences in other pairs? Have the different pairs of autosomes thus different functions in development and inheritance?

We find that the different pairs of autosomes have indeed different functions, and that some characteristics depend on one pair, some on another. This is shown in many cases in which two parents differ in two diverse characteristics. One characteristic may then act as if dependent on one pair of autosomes, the other on another pair. As an example of this, we may take a case studied by Mendel in peas.

One of the original pea plants had seeds that were (1) yellow, and (2) round, or smooth. These, as it turns out, are both dominant characters. The other plants, crossed with those just mentioned, had recessive characters; the seeds were (1) green, and (2) wrinkled.

When these two kinds of pea plants were mated together, it turned out, as we shall see, that yellow and green behave in inheritances as if due to a difference in the two parents in the effects of a certain pair of autosomes; that is, they are alleles. Round and wrinkled behave as if due to a difference between the two parents in the effects of another pair of autosomes. We may therefore represent the two pairs of autosomes in the two parents as in Fig. 29. Representing the dominant characters by capitals, the recessives by lower-case letters, we may in the diagram represent the chromosomes giving origin to the four characters as follows:

A = yellow	a = green
B = round	b = wrinkled

The parents will then be represented as shown in Fig. 29. The germ cells from these parents contain, of course, one member of each pair, as shown in Fig. 29. One parent produces gametes all of the constitution AB, the other gametes all of the constitution ab. When a gamete AB from one parent unites with a gamete ab from the other, all the offspring (F₁)

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thus produced have the constitution $AaBb$, as shown at F_1 in Fig. 29. Since the dominant autosomes A and B are both present, all these individuals are dominant for both pairs of characters; that is, they all have seeds that are yellow and

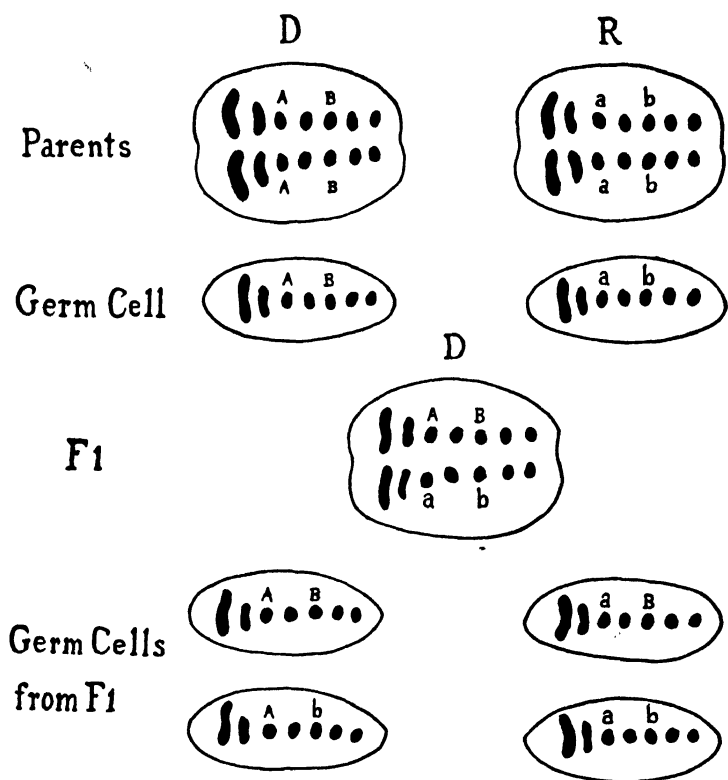


FIG. 29.—Diagram to illustrate the results of mating dominant and recessive parents (D and R) that differ in two pairs of autosomes, AA and BB , aa and bb . F_1 all $AaBb$.

round, as Mendel found. But all are heterozygotes for both of these characters.

Next we mate together two of these F_1 individuals to give the F_2 generation. In forming gametes the rule is, of course, that each gamete contains one member of each pair of

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chromosomes. But the two pairs, Aa and Bb, are distributed to the gametes quite independently. Thus, some get A and B, some A and b, some a and B, some a and b, as shown in Fig. 29.

There are thus from each parent four types of gametes, AB, Ab, aB, and ab, each type being represented by many gametes. The gametes of each of the four types from one parent unite in approximately equal proportions with gametes of each of the four types from the other parent. That is, gametes of the type AB unite in different cases with AB, Ab, aB or ab from the other parent; and so of each of the other gametes of the first parent. The result is to give a set of 16 combinations of gametes (some of which are alike, however, as will be seen). It is not necessary to carry further in our diagram the outlines of the chromosomes. The 16 combinations formed are those shown in the following table:

TABLE 2, FOR INHERITANCE DEPENDING ON TWO
PAIRS OF AUTOSOMES

AB	AB	AB	AB
AB(1)	Ab(6)	aB(7)	ab(5)
Ab	Ab	Ab	Ab
AB(6)	Ab(2)	aB(5)	ab(8)
aB	aB	aB	aB
AB(7)	Ab(5)	aB(3)	ab(9)
ab	ab	ab	ab
AB(5)	Ab(8)	aB(9)	ab(4)

But, as will be observed, not all these 16 are diverse; thus ABAb is the same in constitution or genotype as AbAB. If we number the different combinations, and give the same number to those that are alike, as is done (in parentheses) in the table, we find that there are nine different combinations or genotypes. That is, two parents that are both ABab produce offspring of nine different constitutions or genotypes, in the relative proportions given in the table. When the parents differed in but one pair of characters there were but 3 different combinations. When there are two pairs the number is 3^2 , or 9.

These nine different combinations will manifest the dominant characters A or B, in all cases where an A or B is present

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(whether present once, as *A*, or twice, as *AA*); they will manifest the recessive characters *a* or *b* in all cases in which *a* or *b* is present twice, no corresponding capital letter being present. Collecting together these different types, we find the different characteristics to be manifested in the following proportions of the zygotes:

$$9AB + 3Ab + 3aB + 1ab$$

That is, 9 out of 16 are dominant for both pairs of characters, 3 are dominant for *A*, recessive for *b*; 3 dominant for *B*, recessive for *a*, and 1 out of 16 is recessive for both. There are thus 4 different phenotypes. In Mendel's experiment with peas, in which the two pairs of characters were (1) yellow and green; (2) round and wrinkled; in *F*₁ the proportions were 9 that were yellow and round, 3 that were yellow and wrinkled, 3 that were green and round, and 1 that was green and wrinkled. These proportions hold generally when there are two pairs of characters connected with different pairs of autosomes.

It may be observed that the proportions of the individuals of different constitution or genotype in *F*₂, descended from a cross between parents that differ in respect to two pairs of autosomal characters (so that the parents are *AABB* and *aabb*), can be found directly from the proportions for a single pair of characters. In *F*₂, for the single pairs the proportions are *AA* + 2*Aa* + *aA* and *BB* + 2*Bb* + *bb* respectively. If now we multiply together algebraically these two polynomials, we obtain the relative proportions for the different combinations produced when the two pairs are together. These proportions are the following:

$$\begin{array}{ccccccccc} AABB + 2AaBB + aaBB + 2AABb + 4AaBb + & & & & & & & & \\ (1) & (7) & (3) & (6) & (5) & & & & \\ 2aaBb + AAbb + 2Aabb + aabb & & & & & & & & \\ (9) & (2) & (8) & (4) & & & & & \end{array}$$

Examination will show that this is the same set of proportions shown in table 2 on the preceding page. To bring this out, the same numbers employed in table 2 are placed in parenthesis beneath each combination.

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Certain other relations among the nine different types are important, since they hold for all cases of two pairs of characters that are dependent upon different pairs of autosomes. These are the following:

1. There are four combinations (Nos. 1, 2, 3, 4), *constituting one-fourth of all the zygotes*, that are homozygotes for both pairs of genes. The four homozygotes are diverse in their combinations and in the characters they manifest. They form in table 2 the diagonal from upper left to lower right. Any one of these when self-fertilized or mated with another like itself breeds true: that is, it produces offspring that have the same constitution as the parents.

2. Four out of the 16, or one-fourth of all the zygotes, are heterozygotes for both pairs of characters. They form the class numbered (5), and constitute in table 2 the diagonal from upper right to lower left. Any of these when self-fertilized or mated with another like itself gives again the nine different types, in the proportions above set forth.

3. The remaining 8 in table 2, or one-half of all the zygotes, are homozygotes for one of the two pairs, heterozygotes for the other. Four are homozygotic for A and heterozygotic for B; the other four are heterozygotic for A and homozygotic for B. In these 8 there are but 4 diverse combinations or genotypes, since in table 2 two of each kind are alike. These 4 are numbered above (6), (7), (8), and (9).

If any one of these is self-fertilized, it yields 3 diverse types with respect to the pair for which it is heterozygotic. Thus, the class (6), having the constitution AABb, yields when self-fertilized three combinations in the following proportions:

$$AABB + 2AABb + AAbb$$

The above relations hold for all cases in which two pairs of characteristics are dependent on differences in two different pairs of autosomes, whatever the method of designating the characters or chromosomes.

In a similar way, two parents may differ in three characters that are dependent on three different pairs of autosomes. Such parents could be represented as AABBCC and aabbcc.

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Their progeny (F₁ generation) would all have the constitution AaBbCc. Such F₁ individuals of course produce a variety of germ cells, in accordance with the principles that each germ cell receives one member of each pair of autosomes, and that the different pairs of autosomes are distributed independently. Each parent AaBbCc thus yields the following 8 types of germ cells: ABC, ABc, AbC, aBC, Abc, aBc, abC, abc.

When each of the 8 kinds from one parent unites with each of the 8 kinds from the other, there are produced, of course, 64 groups, which can be arranged in a table like the 16 groups of table 2. If we classify the 64 individuals by the characters which they manifest, we find that there are 8 different phenotypes manifesting respectively the following characteristics:

ABC, ABc, AbC, aBC, Abc, aBc, abC, and abc

That is, some are dominant for all three characters; some for a particular two and recessive for the other; some are dominant for a particular one and recessive for the other two; and some are recessive for all three. The different phenotypes are present in different proportions; the proportions when a large number are examined are as follows:

$$27ABC + 9ABc + 9AbC + 9aBC + 3Abc + 3aBc + 3abC + 1abc$$

The total number of different combinations (genotypes) that occur in such a case is 27, or 3^3 . These combinations can be obtained in their correct proportions by multiplying together algebraically the expressions:

$$(AA + 2Aa + aa) (BB + 2Bb + bb) (CC + 2Cc + cc)$$

Similar but still more complex series are obtained if parents are interbred that differ in four or more characters depending on four or more different pairs of autosomes. If the number of pairs of autosomes is called n , the following relations hold:

If parents differ in n autosomes:

(1) The number of diverse types of gametes produced by the individuals of the F₁ generation is 2^n .

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(2) The number of different combinations (genotypes) in the zygotes of F_2 , formed by mating the 2^n gametes from F_1 , is 3^n .

(3) The number of different phenotypes produced in F_2 is 2^n .

These relations yield very great numbers of diverse combinations, in cases where the number of pairs of autosomes is large. Thus in man, with 23 pairs of autosomes, if all the autosomes differed in the two parents, the number of types of germ cells produced by the F_1 individuals would be 2^{23} , or many millions, the number of possible diverse genotypes in F_2 would be 3^{23} , or many billions, and the number of possible different phenotypes would be 2^{23} . (As will appear later, the number of different possible combinations is greatly increased by the exchange of parts by the members of a pair of chromosomes.)

Thus typical Mendelian inheritance, dependent on differences between different pairs of autosomes, can be treated to a certain extent mathematically. The individuals in F_2 and later generations occur in proportions represented by simple mathematical ratios. These are dealt with in Chapter 9.

It will be worth while to formulate the main facts that we have brought out as to autosomal inheritance:

1. Some single pairs of characters, dominant and recessive, follow in inheritance the method of distribution of a single pair of autosomes.

2. Some pairs of inherited characters follow the rules of distribution of two or more different pairs of autosomes, in the following particulars:

- (a) One member of each pair goes into each germ cell.

- (b) The members of the different pairs are distributed to the germ cells independently, so that all possible combinations containing one member of each pair are formed with equal frequency.

- (c) Each type of gamete from one parent unites with each type from the other parent, the different matings being equally frequent.

METHOD OF DISTRIBUTION OF AUTOSOMES

3. These methods of distribution result, for the characters manifested in the F₂ generation, in certain typical numerical proportions or ratios, known as Mendelian ratios.

4. This method of inheritance is known as Mendelism, or Mendelian inheritance. The rules of Mendelism are the result of the rules of distribution of pairs of autosomes.

5. Most characteristics of organisms are inherited in this way; many more than are inherited in the sex-linked manner. This is evidently because there is but a single pair of X-chromosomes, while there are several or many pairs of autosomes.

6. Thus it is clear that, among the different individuals of a species, there are many different types of autosomes (as there are different types of X-chromosomes), producing many kinds of characteristics.

Other matters connected with autosomes will be taken up in later chapters.

The Y-Chromosome

There remains another chromosome, not included in the autosomes: namely, the Y-chromosome. Has this functions similar to those of X and of the autosomes? Does it too play a rôle in heredity?

As we shall see, the Y-chromosome differs in many ways from the other chromosomes. Let us first summarize the main facts as to the occurrence and distribution of Y-chromosomes.

1. Some organisms have no Y-chromosomes. Among those are many insects (see Fig. 3), the dog, the cat, the horse.

2. In some organisms it is small and appears to be degenerate. This is the case in many insects; also in man (Fig. 19).

3. In some organisms the Y-chromosome is large, but of a different form from its mate X. Such is the case in *Drosophila* (Fig. 7).

4. In some organisms Y is not distinguishable from X in form or size, but experiment shows that it differs from X in function.

5. The Y-chromosome descends from father to son only,

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exclusively in the male line (see Figs. 24 and 25). Normally it never occurs in females.

6. Hence any characters that depend on the presence of a particular kind of Y will (a) be found in males only, and will (b) never be inherited *through* females (since Y does not pass through females).

The Y-Chromosome in Drosophila.—The functions of the Y-chromosome have been more thoroughly studied in *Drosophila* than in any other organism. Most of the facts as to this have already been brought out, in connection with our account of the functions of the X-chromosome. We may summarize as follows the known facts as to the functions of the Y-chromosome in *Drosophila*:

(a) The Y-chromosome, although it normally occurs in males, is not required for the production of male individuals. Through non-disjunction, male individuals are produced that contain no Y (see Chapter 3).

(b) But the presence of Y is necessary for the fertility of males.

(c) Y may exist in females, as a result of accidental non-disjunction; it does not affect their sex.

(d) During many years of intensive study no characteristics were found that follow the Y-chromosome.

(e) But recently it has been shown that the presence of Y prevents the appearance of a certain recessive character ('bobbed') that is due to a modified X-chromosome. This modified X results in the production of shortened bristles on the body of the fly. But this peculiarity does not occur if a Y is present, so that Y has the dominant normal allele for 'bobbed'. Indications of certain other ill-defined functions of the Y-chromosome have of late come to view.

(f) No diverse modifications or defects such as are known in great number for the X-chromosome are known in the Y-chromosome.

(g) Thus in *Drosophila* the Y-chromosome appears to have little function; it seems nearly but not quite inert.

Active Y-chromosomes in certain Organisms; Relation to Male Secondary Sex Characters.—In certain organisms the Y-chromo-

THE Y-CHROMOSOMES

some is more active and varied in its effects. In such cases it shows in different individuals diverse modifications, comparable to the diverse types of the X-chromosome in *Drosophila*, and these produce diverse inherited characteristics that appear in males only.

This matter is closely bound up with the question of what produces the diversity of secondary sex characters. In many animals there are special characteristics which, like the Y-chromosome, are found only in males. These are the male secondary sex characters: horns, mane, beard, greater size, diversities in form, and the like. Since these appear only in the male, the question arises as to whether they may be due to the presence of the Y-chromosome. With relation to this the following is the situation:

1. In most cases, the presence of male secondary sex characters does not depend on the presence of the Y-chromosomes. This is shown by the following:

(a) There are animals which have no Y-chromosome, yet have male secondary sex characters: for example, the dog, the cat, the horse; also various insects.

(b) In *Drosophila*, males that contain no Y (as a result of non-disjunction) have the typical male secondary sex characters.

(c) In some breeds of sheep the male has horns, while the female has none. It could be suggested that this is due to the fact that the male carries the Y-chromosome, while the female does not. But in other breeds, as Dorsets, both sexes have horns, although only the male has the T-chromosome. And in still other breeds, as Suffolks, neither sex has horns, although here as elsewhere the males have the Y-chromosome. If a female of the horned breed (Dorset) is crossed with a male of the hornless breed (Suffolk), in the F₁ descendants the males have horns, although they receive their Y-chromosome from the hornless breed. They have inherited the horns through the mother. Thus it is clear that in these cases the presence of horns is not due to the presence of the Y-chromosome. Extensive work on the inheritance of horns and hornlessness in sheep, goats and cattle² consistently gives results

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which show that the presence of horns is not due to the presence of the Y-chromosome, or of any special type of Y-chromosome.

In all these cases (a), (b) and (c) the presence of distinctive male secondary sex characters depends in some way on the fact that the male carries but one X-chromosome, and consequently produces the male hormone. Their absence from the female results from the fact that she carries two X-chromosomes, and consequently produces the female hormone.

2. But in certain fish, some of the male secondary sex characters apparently do depend on the presence of a Y of a particular type, for they occur only where that type of Y is present, and they can therefore not be inherited through the mother. That is, the Y-chromosomes of certain individuals or breeds are so modified as to produce certain definite characteristics in the individuals that contain them, while individuals that contain another type of Y do not show these characteristics.

An example of this is found in the small fish *Lebistes*.³ In a certain race, the males have a black spot at the base of the dorsal fin, while the females are without the spot. In another race of the same species neither the males nor the females have the black spot. Thus the females of the two races are alike in lacking the black spot, while the males differ. Is this difference the result of differences in the Y-chromosomes of the two kinds of males?

This may be tested by crossing members of the two races. In the spotted race, represent the X and Y-chromosome by capital letters; while in the non-spotted race, represent them by the small letters x and y.

A female of the spotted race, XX, is mated with a male of the non-spotted race, xy, thus:

	Females	Males
Parents	XX	xy
		Non-spotted
F ₁	Xx	Xy
		Non-spotted

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This produces in F_1 females Xx , and males Xy . Neither contains the Y from the spotted race, and neither is spotted. The spot is not inherited through the females of the spotted race.

Next mate the female of the non-spotted race, xx , with a male from the spotted race, XY , as follows:

	Females	Males
Parents	xx	XY
		Spotted
F_1	xX	xY
		Spotted

This yields in F_1 females Xx , and males xY . These males carry the Y from the spotted race, and they are spotted. Thus far the spot goes with the Y from the spotted race.

This Y may be traced further, for example, by breeding together the non-spotted females xx with the F_1 males xY , from the preceding cross, thus:

	Females	Males
Parents	xx	xY
		Spotted
F_2	xx	xY
		Spotted

This gives in the F_2 females xx , and males xY . These males are again spotted; they carry the Y from the spotted race. Wherever this Y from the spotted race is found, the black spot appears; wherever the Y is from the non-spotted race it does not appear. It appears clear therefore that whether the black spot appears in the male depends upon the type of Y -chromosome that it carries. There are two types of Y -chromosome in the species, one producing the black spot, the other not producing it.

It has been shown by Winge⁴ that there are many other colour markings in this fish that depend for their occurrence on the presence of a particular type of Y -chromosome. They occur only in the males, and only in males that have a certain type of Y . In certain other fish also the Y -chromosomes have

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been shown to be diverse in different individuals, giving rise to distinctive characteristics in the male.

In a certain plant, *Melandrium*, also, there are inherited characteristics that depend upon the presence of a particular type of Y-chromosome.

There are some indications also that in man the nature of the Y-chromosome affects certain characteristics. In a family described by Schofield,⁵ the male parent in the first observed generation had webbed toes. This was inherited in the male lines only by all the males for four successive generations. It thus followed exactly the distribution of the Y-chromosome from the original male parent. It seems probable therefore that it is due to a defect or modification in the Y-chromosome of that individual. Many other cases of webbed toes or fingers are known that occur in both sexes, so that they are clearly not due to the Y-chromosome.

On the whole, the situation as to the Y-chromosome and its relation to inheritance may be summarized as follows:

(a) In most organisms Y is a degenerate chromosome, lacking most of the functions manifested by the other chromosomes.

(b) In some organisms degeneration has gone so far that the Y-chromosome has completely disappeared.

(c) In other cases it exists, but is very small.

(d) But in some species the Y-chromosome has effects on hereditary characters that are similar to those produced by other chromosomes. Different types of inherited characters result in such cases from diversely modified Y-chromosomes.

(e) Characteristics dependent on the presence of a particular type of Y-chromosome are inherited in the male line exclusively.

Three main methods of Distribution of Inherited Characteristics.—There exist therefore three diverse systems of distributing hereditary characteristics, depending respectively on the X-chromosomes, the autosomes, and the Y-chromosomes. In each of these the rules of inheritance are given by the special method of distribution of the three types of chromosomes,

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taken in connection with the facts of dominance and recessiveness. Inheritance which follows the distribution of the X-chromosomes is commonly called sex-linked inheritance. That following the distribution of autosomes is known as autosomal or typical Mendelian inheritance. Less important than those just named is Y-chromosome inheritance. All these methods are included under the term Mendelian inheritance, employed in a broad sense.

In some organisms still other methods of inheritance exist; some of these will be presented in later chapters. In higher animals and plants most inheritance occurs in one of the three methods named in the preceding paragraph.

NOTES AND REFERENCES ON CHAPTER 5

1. Page 110. G. Mendel (1866), 'Experiments in Hybridisation', pp. 317-368, in Wm. Bateson's *Mendel's Principles of Heredity* (Cambridge, 1909).

2. Page 127. On the inheritance of horns, see the review by W. Landauer (1925), 'Ergebnisse in der Erbanalyse der Behornung von Rind, Schaf und Ziege', *Zeitschrift für Induktive Abstammungs- und Vererbungslehre*, Bd. 39, pp. 294-322.

3. Page 128. For an account of inheritance through the Y-chromosome in *Lebistes*, see O. Winge (1927) 'One-sided Masculine and Sex-linked Inheritance in *Lebistes reticulatus*', *Journal of Genetics*, vol. 12, pp. 145-162.

4. Page 129. See O. Winge (1927), 'The Location of Eighteen Genes in *Lebistes reticulatus*', *Journal of Genetics*, vol. 18, pp. 1-43.

5. Page 130. R. Schofield (1921), 'Inheritance of Webbed Toes', *Journal of Heredity*, vol. 12, pp. 400-401.

6

CONSTITUTION OF THE CHROMOSOMES

Genes and their Relations to Characteristics

We have seen in preceding chapters that there are many different modifications of a particular type of chromosome, such as the X-chromosome, producing diverse characteristics, which follow in their inheritance the distribution of the chromosome that produces them.

Do all these diverse modifications affect the same part of the chromosome; do they each affect the entire chromosome? That is, does the chromosome act always as a unit, a unit that is diversely modified in different cases, so as to produce different results? Or is the chromosome made up of different parts, with diverse functions: one part being modified when the eye colour is changed, another part when the form of the limbs or of the body is altered, and so on? Are diverse characteristics influenced by different parts of the same chromosome?

Facts have been discovered which show that the chromosome is not a simple unit, but is composed of different parts, with different functions. We shall examine some of the more important of these facts and their consequences, taking the X-chromosome as a type.

As will be recalled, a recessive character that results from a modified or defective chromosome is not manifested when a normal chromosome is present in addition to the modified one. If the cells of an individual of *Drosophila* contain an X-chromosome that is defective in such a way as to cause, when by itself, the wings to be rudimentary, but also contains another X-chromosome that is normal, the wings are not rudimentary, but of the full grown normal type. Or if one

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X-chromosome tends to produce the recessive eosin-coloured eye, while the other tends to produce the dominant normal red eye, the individual bearing the two has the normal red eye.

But what will happen if two X-chromosomes that are so modified as to give different recessive characters are brought together in the same individual? What happens, for example, if in the cells of the same individual there is one X-chromosome so modified as to produce rudimentary wings, and another that is so modified as to produce eosin eyes? This can be brought about by mating a male that has the X defective in one way to a female that has its X's defective in another way. For example, an eosin-eyed mother is crossed with a rudimentary-winged father. Their daughters then contain one X so modified as to produce eosin eyes, the other so modified as to produce rudimentary wings (Fig. 30).

Such matings have been made thousands of times, with many different types of defective chromosomes. The general rule is that in such cases the offspring are quite normal; they have neither of the defects. In the case shown in Fig. 30 the daughters have neither eosin eyes nor rudimentary wings; they are fully normal as to both eyes and wings.

The same result may occur even when the two chromosomes produce defects in the same part or function of the body. Cross together in *Drosophila* two parents, one of which has rudimentary wings, the other having miniature wings, both parents thus strongly defective. The daughters produced, bearing both kinds of defective X-chromosomes, have fully developed normal wings. In the same way, if we cross eosin-eyed individuals with vermilion-eyed (both these colours being the result of defects in the X-chromosomes), the offspring that contain both kinds of defective X's have normal red eyes. Similarly, yellow body crossed with tan-coloured body gives individuals with normal grey body.

Why do two diversely defective X-chromosomes, when brought together in the same egg cell, yield offspring that possess neither of the defects, but are fully normal?

We know that when a normal chromosome is present in the

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same pair with the defective one, the individuals are normal. This suggests a possible explanation. Perhaps the defect is in only a part of the chromosome, and in a different part in the case of diverse defects. Then each chromosome would carry a dominant normal part corresponding to the recessive

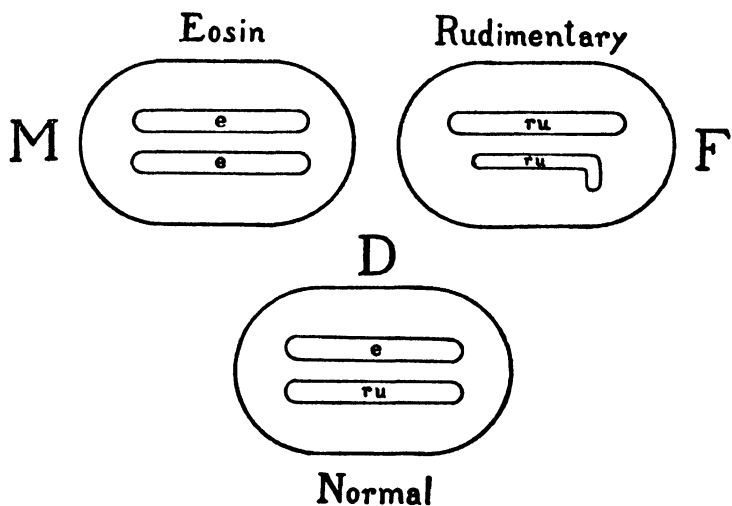


FIG. 30.—Diagram to illustrate the results of putting together two chromosomes that are defective in different ways. *M*, mother; *F*, father; *D*, daughter. The mother's *X*-chromosomes are defective in such a way as to produce eosin-coloured eyes instead of red eyes; the father's *X* is defective in such a way as to produce rudimentary wings. The daughters, receiving an *X* from each parent, have both their *X*'s defective, though in different ways. But they show neither of the defects, having normal red eyes and normal long wings.

defective part of the other. Thus, if the defect that produces eosin eye is in the left half of the chromosome, while that which produces vermilion eye is in the right half, then when the two defective chromosomes are together, there is present a dominant normal left half and a dominant normal right half, so that the individual is normal (Fig. 31, A).

According to this suggestion therefore: (1) The chromosome is composed of diverse parts and a certain part may

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become modified or defective, while the rest remains normal. (2) If one chromosome contains a dominant normal part corresponding to the recessive defective part in the other, the individual produced is normal, so far as this defect goes. (3) Hence when two chromosomes having recessive defects in different parts are brought together, the individual is a dominant normal.

This suggestion we must examine further to determine whether it agrees with the rest of the facts.

An important consequence is to be noted at once. A hundred or more diverse recessive characters are known that are due to modifications of X-chromosomes in *Drosophila*. The general rule is that when any two of these diversely modified X's are brought together in the same cell, the individual produced is normal (certain exceptions will be dealt with later). This would require, according to the suggestion that we are considering, that the X-chromosome is composed of a hundred or more diverse parts. Can this be accepted? There is further evidence on this point, set forth in the following.

Certain other discoveries were made as to the mating of parents having X's that are diversely modified. We know that when two recessive parents having the same modifications in the X's are mated, the offspring all show the same recessive character as do the parents. According to the suggestion we are considering, this is because the two X-chromosomes in the offspring have the same parts modified, so that no corresponding dominant normal part is present (Fig. 31, B). Thus, if the two parents have eosin eyes, all the offspring have eosin eyes.

There have been discovered certain cases in which two X-chromosomes that are somewhat diversely defective do not yield normal individuals when brought together. This is true of certain recessive eye colours in *Drosophila*. If an eosin-eyed mother is crossed with a buff-eyed father, the daughters have both the modified X-chromosomes; yet their eyes are not of the normal red, but rather intermediate between eosin and buff.

According to the suggestion we are considering, this must

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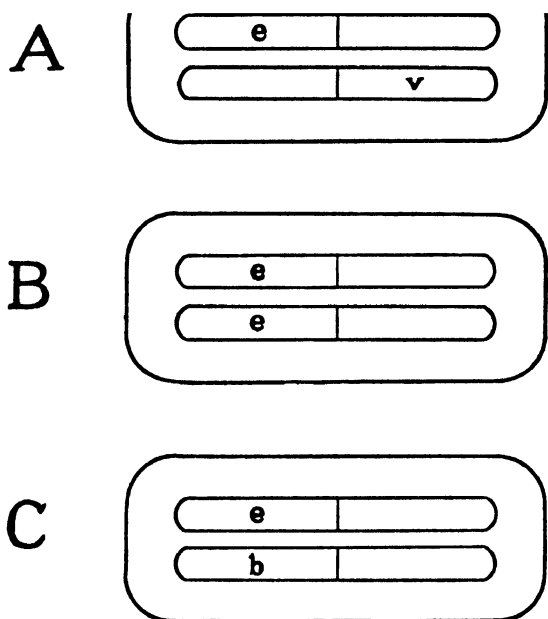


FIG. 31.—*Diagrams to illustrate the suggested explanation of the various different results of placing together two defective chromosomes. The diagrams represent three cells, each containing a pair of chromosomes, each chromosome composed of two parts. A, The two defects (e and v) in different parts of the two chromosomes, so that there is present a normal part corresponding to each defective part. Result, the individual is normal. B, The two defects (e) of the same kind, and present in the same part of the two chromosomes, so that no corresponding normal part is present. Result, the individual manifests the defect e. C, Two different defects (e and b), present in the same part of the two chromosomes, so that no corresponding normal part is present. Result, the individual is defective (usually intermediate between the two defective conditions, but one defect sometimes prevailing over the other).*

be due to the fact that eosin and buff are due to recessive modifications of the same part of the X-chromosomes, so that when the two are together no corresponding dominant nor-

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mal part is present (Fig. 31, C), so that the normal red colour cannot be produced. Several other eye colours have been found to act in this way in *Drosophila*. There is a series of colours, ranging from white through various shades up to near the normal red, each colour being due to a modification of an X-chromosome. The different colours have been named white, ivory, buff, ecru, coral, eosin, tinged, cherry, blood. When any two of these are brought together in the same cell they give, not the normal red, but various intermediate colours. According to the suggestion we are considering, therefore, each of these must be due to a modification of the same part of the chromosome. Different X-chromosomes would have this particular part modified in different ways, so as to yield different eye colours. Is this a credible suggestion?

As we shall see later, it is possible to get other evidence as to whether all these modifications are indeed in the same part of the chromosome.

We have before us then a definite suggestion for examination. This suggestion is that the chromosome is composed of many diverse parts. Any of these parts may become so modified as to produce a recessive character. But if there is present in the cell that same part in the unmodified or dominant condition (in the other chromosome of the pair), then the recessive character is not manifested. How can we discover whether it is true that the chromosome is composed of diverse parts?

Evidence on this is obtained in another way. As we have seen, the sex-linked characteristics resulting from modification of an X-chromosome follow from generation to generation that X-chromosome. Observation shows an extremely important fact. *Sometimes two or more diverse sex-linked characteristics follow the same X-chromosome.* That is, a single X-chromosome is so modified as to bring about two diverse sex-linked characteristics in the individuals that carry it.

For example, certain X-chromosomes cause in the fruit-fly the eyes to be white, in place of the normal red. Certain other X-chromosomes cause the body to be yellow, in place of the normal grey. And sometimes we find individuals that have

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both peculiarities; they have white eyes and yellow bodies. Some of these individuals are males, having but one X-chromosome, so that the two peculiarities must both be due to the same X-chromosome.

And if we breed such male individuals, we find that both these peculiarities are indeed due to the same X-chromosome. Wherever the male's X-chromosome goes, these two peculiarities go with it. They follow that single chromosome for generation after generation, in the complicated course that is followed by the X-chromosome. And in other cases, more than two diverse characteristics are found thus to follow one single X-chromosome. Three, four, five or six have been found following one X-chromosome. And yet, *in other cases, each of these same characteristics is connected with a separate X-chromosome and follows it in its distribution.* That is, two or more characteristics may either be connected with separate X-chromosomes, or they may be all connected with the same X-chromosome. It is to be understood that these are experimental facts, demonstrated in thousands upon thousands of breeding experiments.

In view of these facts, an important question arises. When several characteristics follow a single chromosome, are they following different parts of it? Has the X-chromosome different parts that can be modified separately, as was suggested on other grounds on a former page? Or is the chromosome an inseparable unit, so constituted, however, as to cause in the individual that bears it several different peculiarities?

Experimental breeding answers this question clearly. It is most important to observe what this answer is and how it is obtained, for it constitutes one of the foundation facts of heredity. The answer turns out to be, as we shall see, that the chromosome is indeed composed of different parts, which have different effects in development. These different parts, as we shall see, can be separated, each carrying with it its own peculiar effect. The diverse separable parts of the chromosome having diverse effects are what are called genes. Their existence is solidly demonstrated, and can be verified by anyone who will take the necessary trouble.

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The type of experiment that proves this to be true is as follows: Select in the fruit-fly a male that has white eyes and yellow body. These characteristics are both connected with the single X-chromosome carried by the male, as can be proved by such breeding experiments as have been described above. Now mate such a male with a female whose X-chromosomes are of the usual type, so that she has the dominant normal red eyes and grey body (see Fig. 32). Their daughters (C) get, according to the usual rule, one normal X-chromosome ('red-grey') from the mother, one modified 'white-yellow' chromosome from the father. In the cells of these daughters (C), therefore, these two diverse kinds of X-chromosomes are together side by side in the same cell. And while they are together, as the results show, the two may *exchange parts*, so as to form a new combination of characteristics, thus proving that each is made up of diverse parts.

This is discovered in the following way. Such daughters (Fig. 32, C), carrying the two types of X-chromosomes, are mated with normal males (D), having normal X-chromosomes, and therefore having red eyes and grey body. Observe the sons that they produce (E, F, G, H). These sons, as we know, receive their single X-chromosome from their mother only, getting only the Y from the father. The two X-chromosomes of the mother separate, as we know, into different eggs. The eggs that contain the normal or 'red-grey' X-chromosome, when fertilized by a Y sperm of course produce sons with red eyes and grey body (E, Fig. 32). The eggs with the recessive 'white-yellow' X-chromosome (which came from the original male B, Fig. 32), produce sons with white eyes and yellow body (F). Most of the sons produced are of these two types, in equal numbers. But, in addition, there are a few sons (about one per cent of all) that have a new combination of characteristics. There are a few sons that have red eyes and yellow body (G, Fig. 32). And there is an equal number that have white eyes and grey body (H). It is clear that in the single X-chromosome of these sons a new combination has been made, composed of a part of the X-chromosome of the original father (B), and a part of the X-chro-

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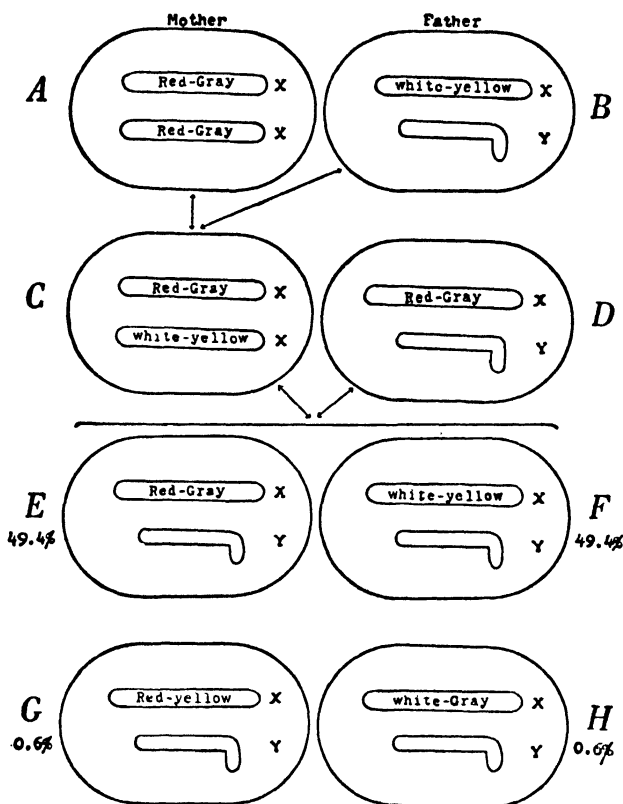


FIG. 32.—Diagram of results of breeding which show that the X-chromosome consists of separable parts having different effects on development. A female A, whose X-chromosomes yield red eyes and grey body, is mated with a male B whose single X-chromosome yields white eyes and yellow body. Their daughters C have together in the same cell the two kinds of chromosomes, one yielding red and grey, the other white and yellow. In some of the cells of such daughters these chromosomes exchange parts, so that one now produces red eyes and yellow body, the other white eyes and grey body. This is demonstrated by the fact that such daughters produce a number of sons (G and H) whose single X-chromosomes yield these new combinations together with many sons (E and F) in which the single X-chromosome produces the original combination of characteristics.

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mosome from the original mother (A). The mother's X and the father's X have exchanged parts, in some cases, while together in the cells of the daughters; the exchange has occurred in about 1 to $1\frac{1}{2}$ per cent of them, not in the others. The newly combined chromosomes behave in later generations just as did the original combinations. The new combinations (red-yellow and white-grey) follow in later generations particular single X-chromosomes.

In this formation of new combinations, it is clear (1) that two characteristics that were connected with different X-chromosomes (as red eyes and yellow body) later become combined with a single X-chromosome; and (2) that characteristics that were first connected with a single X-chromosome (as white eye and yellow body) have later become separated, so as to be connected with two different X-chromosomes. It is clear, therefore, that the white and the yellow are connected with different parts of the chromosome, and that these different parts can be separated.

This same process of forming new combinations of parts of previously existing X-chromosomes has been found to occur (as we shall see later) with any of the other hundred or more diverse kinds of X-chromosomes that are known to occur in *Drosophila*. The process of exchanging parts of the chromosomes is commonly spoken of as 'crossing-over' of a part from one chromosome to another. So remarkable a process has of course attracted the attention of many investigators, and it has been studied in hundreds of thousands of cases. Details concerning it we take up later.

All this answers the question, proposed earlier, as to whether the chromosome is a simple unit, or is composed of a number of different parts with diverse functions. The chromosome does indeed consist of diverse parts that may become separated. And it is clear that these diverse parts have different functions, different effects on development. One part of the X-chromosome of the original father, in the experiment we have described, causes the eye to be white; another part causes the body to be yellow; and these parts can be separated. In the original mother, one part of the chromosome

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caused the eyes to be red, another part caused the body to be yellow; and these parts also can be separated. Different parts of the chromosome affect different characteristics.

In a later chapter it will be shown that the chromosome may by means of radiation be broken into two or more visible pieces, and that the different pieces produce the diverse characters that are ordinarily connected with the single chromosome. The relations shown in the exchange of parts by two chromosomes, described above, are fully confirmed by the results of physically breaking the chromosome into pieces.

The separable parts of the chromosome, with diverse functions, are known as genes. It is important to observe that the existence of the genes, as separable parts of the visible chromosomes, is definitely proved by experimentation. Genes are not mere hypothetical units with imaginary properties, as is sometimes asserted. Genes are separable parts of the chromosomes, having diverse effects on development; their existence is solidly demonstrated, and can be verified by anyone who will take the necessary trouble. There is of course room for theorizing, in the present state of our knowledge, as to the precise nature and action of genes, but this does not touch the fact of their existence and effects.

How many separable parts are there in the chromosome? That is, how many genes are there? And how are they arranged; how are the parts put together to form the chromosome? And how is their number and arrangement discovered?

These questions are answered through an examination of the processes of exchange of parts of the chromosomes, in the case of different sets of characters. The evidence is somewhat complex, although entirely clear in its bearings on the questions once it is completely mastered. It will be possible to present only some of the main features of the evidence. If this is followed with care it will give an understanding of some of the essential features of the materials of heredity that can be obtained in no other way. The relations to be brought out are fundamental for a correct understanding of heredity; they should on no account be neglected by the student.

Go back first to the experiment illustrated in Fig. 32. In

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this experiment, a 'red-grey' X-chromosome from the mother (A) and a 'white-yellow' X-chromosome from the father (B) were brought together in the cells of the daughters (C). There, as is shown by the nature of the sons (E, F, G, H) produced by these daughters, in a small proportion of the cells the two chromosomes exchange parts, so that sons with four different types of X-chromosomes are produced, in place of the two original types that were present in the cells of their mothers (C). The proportion of the cells in which exchange has occurred is directly shown by the proportion of the sons that have the new combinations, red-yellow and white-grey. When this experiment is performed with thousands of individuals (as has often been done), the percentage of the different combinations among the sons is found to be approximately the following:

Red-grey	49·4
White-yellow	49·4
Red-yellow	0·6
White-grey	0·6

The new combinations are the Red-Yellow and the White-Grey, and together they form about 1·2 to 1·5 per cent of all. That is, exchange or crossing-over has occurred in about 1·5 per cent of the cells of the mothers (C), while in the other 98·5 per cent it has not occurred.

This proportion in which exchange has occurred is known as the exchange ratio, or as the cross-over ratio. This exchange ratio plays a most important rôle in the evidence on the questions with which we have to deal.

Constancy of the Exchange Ratio for a given Pair of Characteristics.—Approximately this same exchange ratio is produced whenever this particular mating is made in a large number of cases. If by such matings a thousand sons are produced, and this is repeated, in each 1000 there will be about 985 to 988 showing the original combinations, about 12 to 15 showing the new combinations. If the original parents show the reverse combinations (red-yellow and white-grey), then the new combinations red-grey and white-yellow will appear in

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about 12 to 15 cases out of each 1000. Thus for a given pair of characters (as white-yellow) the exchange rate is approximately constant.

Diverse Exchange Ratios in different Pairs of Characteristics.—If, in place of the characteristics we have been considering, some other pair of recessive characteristics is crossed with normals, a different constant exchange ratio is produced. Thus, if individuals with yellow body and bifid wings (characters connected with the X-chromosome) are mated with normal individuals (having grey body and normal wings), and the second generation is obtained in the way illustrated in Fig. 32, the sons show an exchange ratio of about 5·3 per cent. And this ratio is produced, approximately, whenever this pair of characteristics is tested.

A Series of Diverse Exchange Ratios.—Still other pairs of characteristics give still different exchange ratios. If matings are made using many different pairs, many different exchange ratios are produced. It is particularly instructive to examine the ratios for a series of pairs, one member of which is the same in each case. Taking white eyes as the member that is the same in each case, the following series of exchange ratios is found when in *Drosophila* white is paired with different characters, and individuals bearing the two are mated with normals:

White—Abnormal abdomen	1·7
White—Bifid wings	5·3
White—Club wings	14·3
White—Vermilion eye	30·5
White—Miniature wings	33·2
White—Rudimentary wings	41·2
White—Bar-eye	43·6

The exchange ratio of the character white eye with many other characteristics has been determined, but the above list gives typical results. There is a whole series of diverse exchange ratios, varying from about one per cent to nearly 50 per cent—each ratio being approximately constant when the given pair of characteristics is employed.

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Why does there exist such series of diverse ratios as is illustrated above? When there is an exchange, the two parts of the given chromosome that produced the two characteristics become separated from each other; they break apart. If the exchange ratio is low, they break apart only in rare cases; if the exchange ratio is high, they break apart frequently. The question then becomes: Why do certain parts of the chromosome break apart frequently, others less frequently, in the way shown by the series of exchange ratios?

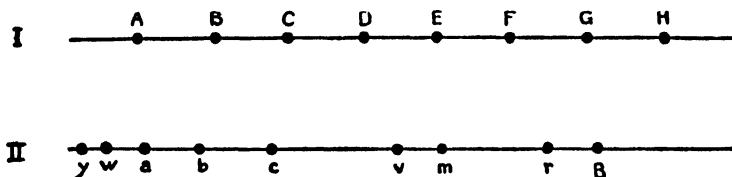


FIG. 33.—*Diagrams to illustrate the arrangement of genes in linear series. I, Genes A to H (see text). II, The order of the genes producing yellow (y), white (w), abnormal abdomen (a), bifid wings (b), club wings (c), vermilion eye (v), miniature wings (m), rudimentary wings (r), and bar-eye (B), according to the theory of linear arrangement of genes.*

In judging of this, there are certain important facts to be considered:

1. It can be proved experimentally that the exchange of parts occurs at the time of the last two divisions in forming germ cells (see Fig. 17). (This is proved by subjecting the individuals at different periods in their lives to high temperatures, which change the frequency of exchanges. This result occurs only if the subjection to high temperatures occurs at the time mentioned.)

2. At this period the two chromosomes are side by side, in conjugation.

3. And each is seen to be a slender elongated thread, having thickenings at intervals, in linear series (Figs. 36 and 37).

4. The breaking apart and exchange of parts therefore occur in these long slender threads.

5. Possibly, therefore, the differences in the frequency of

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separation of different parts of the thread are due to the fact that some parts are close together on the thread, others far apart. If the chromosome breaks in but one or two places, as appears to be the case, parts that are far apart would become separated more frequently than parts that are close together.

Represent the chromosome by a line on which there are consecutive thickenings, A, B, C, . . . to H, representing genes (Fig. 33, I). Then if a break occurs anywhere in the chromosome it will separate the extreme genes A and H. But to separate any two adjacent genes, as E and F, a break must occur precisely in the short stretch that lies between them. Any break that separates two genes that are near together will separate others lying farther apart. The result of these relations is that the farther apart in the series two genes lie, the greater would be their frequency of separation, and consequently their exchange ratio.

The suggested answer to the questions is then as follows: The exchange ratios are different for the different pairs of characters, because the genes to which these characters are due are at different distances apart on the thread-like chromosome. Two genes that are close together give a small exchange ratio; two genes that are farther apart give a larger exchange ratio. The greater the ratio the farther apart are the genes. These relations therefore yield a series of diverse ratios, as seen in the list on page 144.

Is this suggestion borne out by the known facts as to the chromosomes and as to the crossing-over of different genes? Let us examine the facts from this point of view.

In accordance with this suggestion, the genes on which depend the characters in the list on page 144 would be arranged in series in the order of the ratios which they give with white. If we think of white as at one end of the series, then the genes would be in the order: white, abnormal, bifid, club, vermilion, miniature, rudimentary, bar, as shown in Fig. 33, II.

Certain consequences of this idea appear at once, and these may be used for testing whether the idea is adequate.

1. Since the size of the ratio depends on the distance apart

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of the genes, two genes that have nearly the same ratio with another must be at about the same distance from it. Thus vermilion, with a ratio of 30.5 from white, must be at nearly the same distance from white as is miniature, since the latter has a ratio of 33.2. If white is at the end of the series, therefore, vermilion and miniature must be close together. And if they are close together, they must have *with each other* a small exchange ratio. This can be tested; it has been done on a large scale. The exchange ratio for vermilion-miniature is found to be indeed small, about 3.1 per cent. This same relation is found for other characters that have similar relations with white. A large number have been tested, in addition to those mentioned in the list. In all cases, characters that have nearly the same ratios with white have together small ratios; while characters that have very different ratios with white have together large ratios. This agrees completely with the idea that we are testing. All the relations found between the ratios are such as are to be expected if white is near one end of the chromosome, and the other genes in the list are so placed in the linear series that the near ones give small ratios, the more distant ones large ratios.

Of course, if the gene for white were not near one end of the chromosome, two other genes might be at equal distances from it, but on opposite sides of it, so that they would be far apart, and would therefore together have a large exchange ratio. All the evidence, however, is that the gene for white is near one end of the chromosome (though not quite at its tip), so that all the genes in the list on page 144 lie in the same direction from white. There is evidence, however, that the gene yellow, which has with white the ratio 1.5, lies on the other side of white, close to the very tip of the chromosome, as shown in Fig. 33, II.

2. But if the ratios of the other genes are taken with vermilion, for example (Fig. 33, II), we find exemplified the relation just mentioned: genes that have nearly the same ratio with it may behave as if they were on opposite sides of it, and so have together a large exchange ratio. In all these respects the relations are what is to be expected if the genes

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are in a linear series, and their distance apart determines the magnitude of the exchange ratios between them.

3. A most important consequence of the idea that the genes are in a linear series, and that crossing-over is due to breaks and exchange of parts in the thread-like chromosome, is as follows. When the chromosome breaks in such a way as to separate, into different chromosomes and different individuals, two genes such as club and miniature in Fig. 33, II,

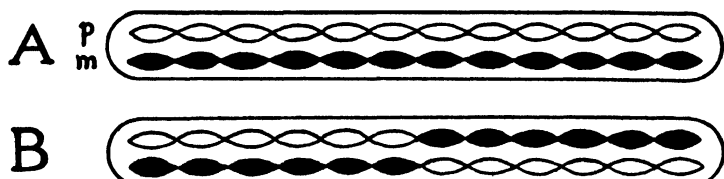


FIG. 34.—Diagram to illustrate crossing-over. In A, the paternal (*p*) and maternal (*m*) chains of genes. In B (a later stage), a part of the chain *p* (white) has become united with a part of the chain *m* (black); the two have exchanged part of their genes.

then all the genes on one side of the break must go together to one individual, while all those on the other side of the break must go together to the other individual. Thus, in case of a break between club and vermilion (Fig. 33), the genes for yellow, white, abnormal and bifid would go with club to one individual, while the genes for bar, rudimentary and miniature would go with vermilion to the other individual. Crossing-over would therefore not be confined to single genes, but would occur in blocks; and the genes that go together could be predicted from a knowledge of the exchange ratios of the genes.

This furnishes a crucial test of the theory, for if the genes are not in a linear series this relation is not to be expected. Examination shows that the requirement set forth in the preceding paragraph is indeed fulfilled. Crossing-over actually does occur in blocks of genes, those shown to be near together in the linear diagram (Fig. 33) going together to one individual; while a block of those that are together in a distant part of the series go to the other individual. Fig. 34 is a diagram showing what occurs at crossing-over.

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As to the intimate processes that occur in the chromosomes, when exchange occurs, the following facts are known:

A. The exchange of parts occurs while the chromosomes are conjugating in the process of forming germ cells.

B. They are then in the form of long threads, with corresponding thickenings on the two threads (Fig. 37). These thickenings probably show the location of genes.

C. These threads become closely united; they are seen under the microscope to be intimately intertwined.

D. Later they separate, and study of the characteristics of the individuals produced from the germ cells, as described earlier, shows that at a certain point the original threads have broken, so that part of the thread *p* has become united with the remainder of thread *m*, as shown at B in Fig. 34. Thus a consecutive series of genes from chromosome *p* has become united with a similar series from chromosome *m*, as shown in the figure.

Thus far, all the relations we have examined agree with the idea that the genes are arranged in the chromosome in a consecutive series, and that crossing-over occurs by break and exchange of parts in two such threads.

Certain relations brought out on earlier pages furnish further tests of this theory.

4. On page 133 it was seen that when two chromosomes that are defective in different ways are united in the same cell, by mating parents bearing the two kinds of defects, the offspring produced are usually dominant normal. The reason suggested was that the two recessive defects are in different parts of the two chromosomes (Fig. 31, A). Therefore each chromosome supplies a dominant normal part or gene corresponding to the recessive gene of the other, so that the individual is normal. In view of the known fact that there are many genes in the chromosomes, these relations can be illustrated as in Fig. 35. If *a* and *k* are the two defective genes, chromosome 2 supplies a dominant gene *A* corresponding to the defective gene *a*, while chromosome 1 supplies a dominant gene *K* corresponding to the defective gene *k*.

Note now the relation of these facts to the exchange ratios.

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If two chromosomes with defective genes (as *a* and *k* in Fig. 35) yield normals, the defective genes are conceived to be in different parts of the chromosomes. They would therefore be at different distances from any third gene, as *T* in Fig. 35. And since the exchange ratios depend on distances, they should give different exchange ratios with that third gene. The gene *k* would give with *T* a smaller ratio than would the gene *a*. In general, when two recessive genes in different chromosomes yield dominants, the two recessive genes should have diverse exchange ratios with any third gene.

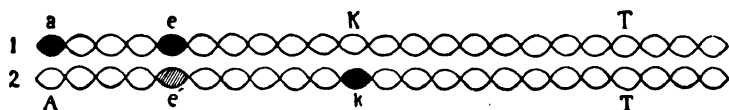


FIG. 35.—Diagram to illustrate certain relations in crossing-over, or the exchange of parts of the chromosomes. The oval bodies represent the genes. See text.

Is this in fact the case? Experimentation shows that it is. For example, in *Drosophila*, vermilion eye and eosin eye mated together give normals. The yellow-vermilion ratio is 34.5; the yellow-eosin ratio is 1.5. It is clear, therefore, that vermilion and eosin are in diverse parts of the chromosome.

This turns out to be a general rule. When two recessive genes in different chromosomes give when brought together a dominant or normal individual, these two recessive genes have diverse exchange ratios with any third gene, showing that they are in different parts of the chromosomes.

This relation becomes of particular significance when it is contrasted with another, to be taken up next.

5. In some cases, as set forth on page 135, two diverse defects in different chromosomes do not yield normals when the two chromosomes are brought together in the same individual. Instead, they yield a defective condition that is usually intermediate between the defects due to the chromosomes taken separately; or they yield a condition that approaches one of these defects more closely than the other. Thus when the chromosome that produces eosin eye is brought together

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with that which produces coral eye, the two give, not the normal red eye, but an eosin-coral eye.

This, it was suggested, is because the two recessive defects must be at the same point in the chromosome; they must affect corresponding genes of the two chromosomes, two members of the same pair, such as e and e' in Fig. 35. In consequence, when the two are together (as in Fig. 35), both genes of that pair are defective; no corresponding normal gene is present, so that a normal individual is not produced.

This situation again furnishes a test of the idea that the genes are in linear order. For if the two defective genes are indeed in the same gene pair (e and e' , Fig. 35) then the two must, according to the linear theory, be at the same distance from any third gene, as A or T , and therefore they *must give the same exchange ratio with any third gene*.

This can, of course, be tested experimentally in such an organism as *Drosophila*; it has been done in many cases. In the example we have mentioned, eosin eye and coral eye both give with yellow body the exchange ratio 1.5 per cent. It is therefore true that they are located in the same part of the chromosome. The two also give the same ratios when tested with any other gene: for example, their exchange ratio with vermilion eye is about 33 per cent. There is a whole series of eye colours in *Drosophila* that acts in the way just described. Any two placed together give, not the normal eye colour, but an intermediate condition. And all of them have the same exchange ratio with any third gene. Their exchange ratio with yellow body is 1.5 per cent, their common exchange ratio with vermilion eye is 33 per cent. They are all therefore different modifications or defects of the same part of the chromosome, the same gene. This series of eye colours has been mentioned before; it includes white, ivory, buff, ecru, coral, eosin, tinged, cherry, blood.

Such a series of diverse modifications of the same gene is commonly spoken of as a set of multiple allelomorphs or alleles. Many such sets of recessive multiple alleles are known in different organisms. They all show the same peculiarities. Any two (in different chromosomes) can be brought together

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into the same individual, giving, not the normal dominant characteristic, but a mixed or intermediate condition. And all the members of any such set have the same exchange ratio with any third gene, indicating that all are due to modifications of the same gene.

All of this agrees, as will be seen, with the theory that the genes are arranged in a consecutive series, and that different exchange ratios are the consequence of the different distances between genes that are tested. Hence, characteristics that are due to modifications of the same gene have the same exchange ratios with any other; while characteristics that are due to modifications of different genes have diverse ratios with any other.

6. There is a further important fact which again tests the adequacy of this idea of the arrangement of the genes. Two genes that are in different parts of the two chromosomes of the same pair can be brought by crossing-over into the same single chromosome. Thus, in Fig. 35, by a break and exchange of parts occurring in the region between the gene pairs *aA* and *Kk*, the two genes *a* and *k* would be brought into the same chromosome. On the other hand, two genes that are in the corresponding parts of the two chromosomes of a pair, as for example *e* and *e'*, cannot be brought by crossing-over into the same chromosome, because the break is always at the same point in the two chromosomes of a pair, as illustrated in Fig. 34.

The facts shown in breeding experiments agree precisely with these relations. Any two recessive genes that yield dominants when brought together into the same cell must, as we have seen, be at different regions of the two chromosomes (like *a* and *k* in Fig. 35), and it is true that any two such recessive genes can by exchange be brought into the same chromosome. Thus, in the X-chromosome of *Drosophila*, if white eye is originally in one individual, yellow body in another, each connected with an X-chromosome, the two may be brought by crossing-over into the same single X-chromosome, as illustrated in Fig. 32, page 140. Thus they can both be present in a male which has but one X-chromosome in his cells. Similarly, eosin eye and vermilion eye can be

brought together into the same X-chromosome. In general, it is true that *any two recessive genes that yield dominants, when brought together into the same cell, can, by crossing-over, be brought into the same chromosome* (where of course they occupy different places).

On the other hand, it is an experimental fact that recessive genes that do not give dominants when brought together into the same zygote (and therefore must be at the same location in the two chromosomes) *cannot be brought into the same chromosome*. They are thus never present in the same male, since the male has but one X. Thus, eosin eye and coral eye cannot both be present in the same X-chromosome, though eosin eye and vermilion eye can. These, it will be understood, are experimental facts; many thousand experiments have given these results. Of the entire series of multiple allelomorphs, white—ivory—buff—coral—eosin—ecru—cherry—blood, etc., no two, it is found, can ever be brought together into the same X-chromosome; no two can ever be present in the same male, though any two can be present in the same female (which has two X's).

This again of course agrees with the conception, originally based on other grounds, that all these are modifications of the same gene. When the chromosomes conjugate, the corresponding parts or genes of the two lie opposite one another, and the break which results in exchange of parts occurs at the same point in the two (Fig. 34). Thus two genes of the same pair are not brought together into the same chromosome.

7. The validity of the conception that the genes are arranged in a chain can be tested by breaking the chromosome, through the use of radiation. This is a matter that will be taken up in a later chapter; here we give only a general statement of the relation of the broken chromosomes to the linear arrangement of the genes. By the methods already described, the order of the genes in the chromosomes is determined, so that maps may be made showing this order, as illustrated in Fig. 38. In *Drosophila* it is shown in this way, for example, that the genes producing yellow body, white eye, abnormal abdomen and bifid wings are near one end of the X-chromo-

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some, that those for vermilion eye, miniature wing and furrowed eye are near the middle of the chromosome, and that those for bar-eye, cleft wings and bobbed bristles are near the opposite end of the X-chromosome from that which carries the genes for yellow body and white eyes. When individuals are subjected at the proper stages of development to X-rays, the chromosomes in their germ cells are frequently broken, and the broken chromosomes can be detected under the microscope in the cells of the offspring of the radiated individuals. Sometimes thus a small piece of one end of an X-chromosome is broken off; it may then become visibly attached to one of the autosomes. In such a case the characteristics dependent on the genes in this piece of X change their method of inheritance in later generations; they are now distributed to offspring by the method of autosomal inheritance, instead of by sex-linked inheritance; for now they are attached to an autosome. It is therefore possible by study of the inheritance in later generations to determine what genes are present in the piece of X that is broken off. Such determinations have been made in many cases.

The results of these studies show that the order of the genes shown on such maps as Fig. 38 is correct. When a small piece of the end of the X-chromosome is broken off, such study as we have described shows that it contains the genes for yellow body, white eyes, and the other genes near the tip of the chromosome. If a longer piece of X is broken off, it contains more of the genes—those extending farther toward the middle of the chromosome. Such studies, with the X-chromosome and with the autosomes, have been made on a large scale in *Drosophila*; they confirm throughout the order of the genes shown on the maps, the order originally determined by study of the different exchange ratios of the genes, as described in the foregoing pages.

Thus, in sum, all the tests to which the matter has been subjected agree with the conception that the chromosome is composed of separable genes, having different effects on development and characteristics; that these genes are arranged consecutively, like beads on a string; and that the

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different exchange ratios of different pairs of genes are due to the different distances of the genes one from another.

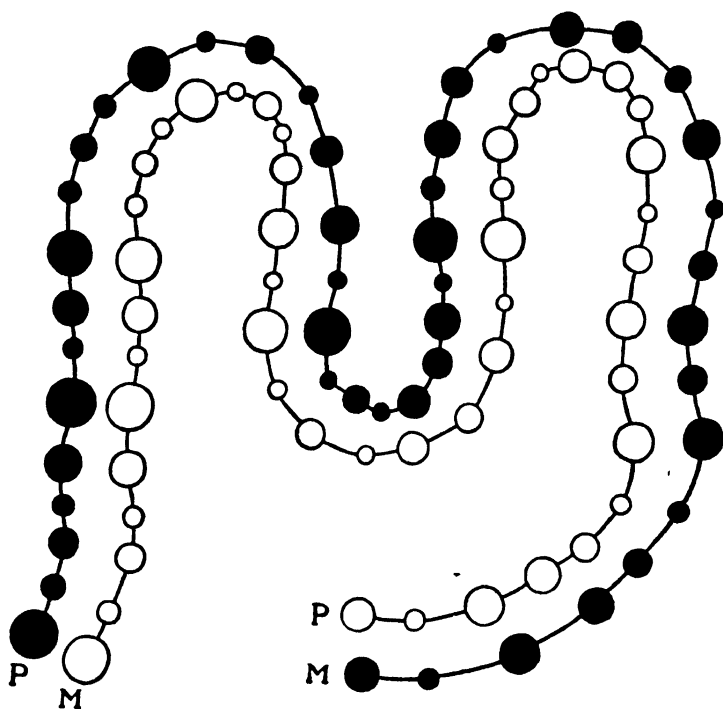


FIG. 36.—Diagram to illustrate the arrangement of the genes in the genetic system. The genes, represented by the circles, arranged in consecutive order in long paired strings which are the chromosomes. One series (P) is derived from the father, the other (M) from the mother. Thus the genes are in pairs, one member of each pair from each parent, the two members of each pair having analogous functions, though one may be dominant, the other recessive.

This conception is subject to test in many other ways that cannot be described here. The consecutive arrangement of the genes results in many diverse mathematical relations, which must hold in the results of experimentation, if the consecutive order is correct. It may be stated that the results of

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literally hundreds of thousands of experiments show that these relations do hold, and they agree with and confirm this consecutive arrangement of the genes. Furthermore, the chromosome is seen under the microscope to be, at the time when crossing-over occurs, a linear structure with consecutive thickenings (Fig. 37); in other words, just such a structure as the results of experiments show it to be.

It may, therefore, be considered established that this conception is correct. The arrangement of the genes may therefore be represented as in the diagram of Fig. 36. The genes in any zygote form two series, one series derived from the father, one derived from the mother. The two series (P and M, Fig. 36) contain corresponding genes. Thus the genes are in pairs, each pair containing one gene of paternal origin, one of maternal origin. The two genes of a pair have corresponding functions, though one may be dominant, the other recessive; one normal, the other defective.

This arrangement of the genes is one of the fundamental facts of genetics, which must be thoroughly grasped if the results of inheritance are to be understood. The arrangement of the genes in chromosomes; the fact that those thus together in the same chromosome usually go together into the same germ cell and the same individual; the fact that sometimes exchange of genes occurs between the two chromosomes of a pair; the fact that the frequency of exchange is greater the farther apart the genes are in the string of genes—all these have most important consequences in inheritance and variation as generations pass. No one who neglects them can have an adequate understanding of the phenomena of heredity and variation, of similarity and diversity among individuals. These relations play a most important rôle in the further account of genetics given in the remainder of this book.

Can the genes be seen under the microscope? During the formation of germ cells, at the time when the crossing-over of genes occurs, the chromosomes are seen to be linear structures, with consecutive thickenings (chromomeres), the two thickenings of the conjugating pair of chromosomes side by side, as shown in Fig. 37. While it is impossible to prove that

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these thickenings represent or contain the genes, it seems probable that they do. For their arrangement is exactly that which experimentation shows must be the arrangement of the genes.

Maps of the Chromosomes.—Since the genes are thus known to be in serial order, maps can be made of them, provided there

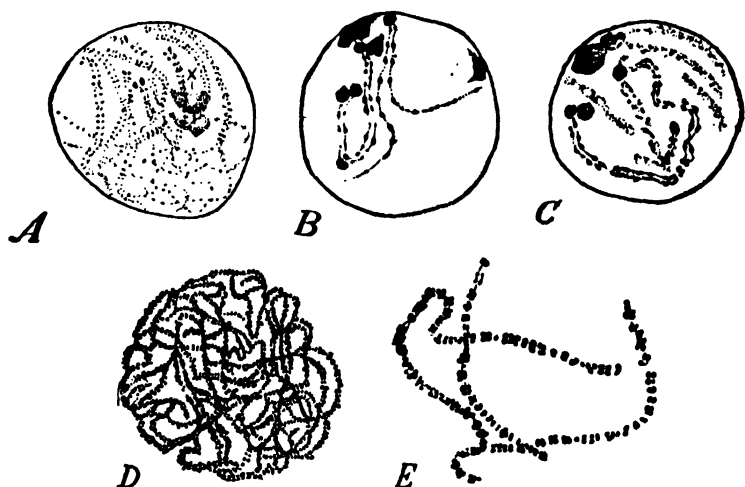


FIG. 37.—Structure of chromosomes as seen under the microscope, showing the minute paired particles or chromomeres, of which each is composed. The chromomeres presumably represent the genes. A, B, C, chromomeres in the chromosomes of the grasshopper, after Wenrich. The paired condition of the chromomeres (genes?) is clearly shown. In B, the two members of one of the chromosome pairs are approaching each other in conjugation, but are not completely conjugated. D, E, chromomeres (genes?) in the chromosomes of the lily, after Belling. E shows a portion of D at higher magnification.

is a sufficiently detailed knowledge of the genetics of the organism in question. Such maps show the order of the genes in the chromosomes. In making such maps the guiding principle is the fact that two genes having together small exchange ratios are close together, and that the larger the exchange ratio between two genes the farther they are apart. Such maps of the chromosomes of *Drosophila* are shown in Fig. 38.

The position of a gene on the map or in the chromosome is

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known as its *locus*. The locus of any gene is defined by its distance in certain units of length from one of the ends of the chromosome, the upper or 'left' end in the maps being that selected as the point of reference. Each unit is such a chromosome length as gives, for two genes at opposite ends of it, exchanges in one per cent of all cases (thus it is a trifle less than the distance in the X-chromosome from the gene yellow to the gene white, which exchange is about 1.5 per cent of all cases). To designate the locus of a gene, it is common to specify the chromosome in which it occurs (I, II, III or IV) and its distance in units from the upper end of the chromosome. Thus, in the X-chromosome, which is number I, the gene white is at the locus I, 1.5; the gene miniature at I, 36.1. The gene purple is at II, 54.5; the gene sepia at III, 26.0, and so on.

Such maps when carefully made can be depended on as showing correctly the order of the genes, and approximately their relative distances apart. The relative physical distances apart, as would be seen under the microscope, differ somewhat from those shown on the map, because the frequency of exchange is somewhat greater in some parts of the chromosome than in others. Also, the frequency of the breaks and exchanges in the chromosomes is known to be affected by a number of other conditions besides the distances separating the genes. Yet on the whole the relations shown by the map are sufficiently near to those actually occurring to make the maps of great value. They are extremely useful in helping to understand and predict the course of inheritance. From them can be determined the proportions of descendants that will show certain combinations of characteristics, when the combinations occurring in the ancestors are known, as will be brought out in later pages.

Maps of the chromosomes have been made for only a few organisms thus far, particularly for two or three species of *Drosophila*. Beginnings have been made for the chromosomes of maize, the pea plant, the sweet pea, the rat and mouse. For most organisms the experimental data are as yet too scanty to permit even the beginnings of chromosome maps to be made. This is notably the case for man. His 24 pairs of chromosomes,

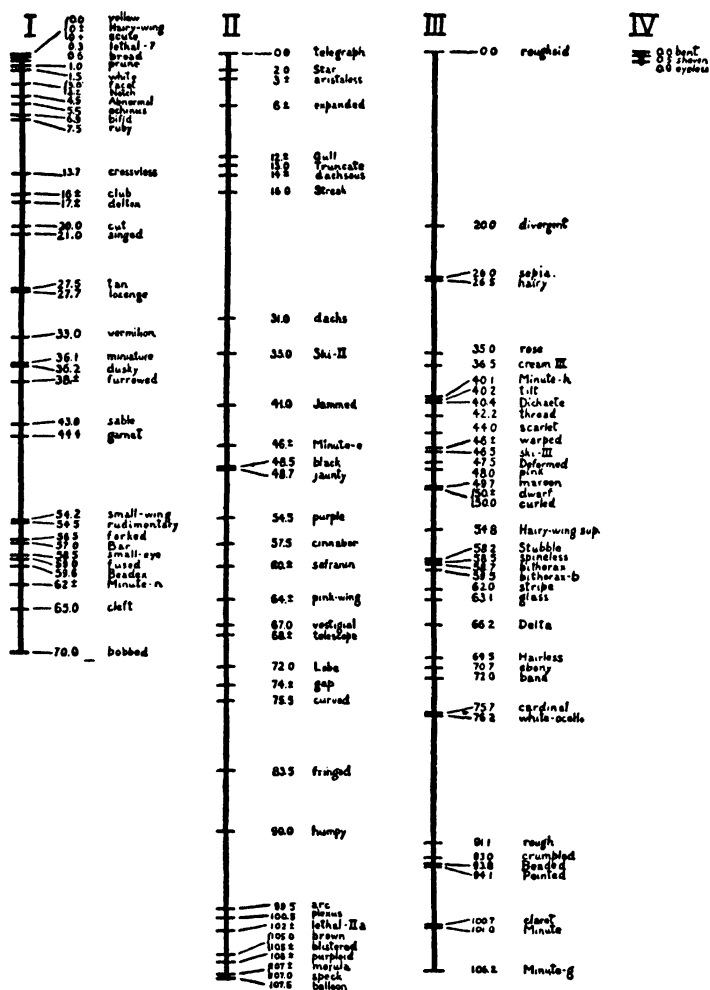


FIG. 38.—Maps of the four chromosomes of *Drosophila melanogaster*, after Morgan, Bridges and Sturtevant, *The Genetics of Drosophila*. The genes are named for certain bodily characteristics which they produce when modified in a certain way. Names beginning with a lower-case letter are recessive genes; those beginning with a capital are dominant. The numbers opposite each name show in units of equal length the distance of the gene from the upper (or 'left') end of the chromosome. In the spaces between the indicated genes are presumably other genes, not yet studied.

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together with the fact that experimental breeding cannot be carried on in man, will make the preparation of maps of his chromosomes a difficult if not impossible task.

Place and Frequency of Breaks in the Chromosomes.—Certain important points have been discovered as to the frequency of breaks, the number of breaks, and their location, in the exchanges that occur between the two members of a pair of chromosomes. The evidence for these cannot be given here, as it is detailed and voluminous, but the main facts may be summarized. It will be recalled that the breaks and exchanges occur in the germ cells at the time when the two chromosomes of a pair are side by side as long threads (Fig. 37, A, B, C).

1. In the different cells of even the same individual, the chromosomes of any type, as X, or a particular autosome, show breaks in different numbers and locations.

2. In some of the cells the chromosome does not break, so that there is no exchange. This is, as a rule, the case in a rather large proportion of the different cells.

3. In some of the cells the chromosome breaks in but one place, so that, if we designate one of the chromosomes p , the other m , a single continuous piece of p including one end is transferred to m ; a similar piece of m to p (Fig. 34).

4. In a small proportion of the cells the chromosome breaks in two places, so that a piece from the middle portion of p is transferred to m , and vice versa.

5. Very rarely the chromosomes break in three places, so that there is exchange of two separate pieces. More than three breaks are extremely infrequent.

The consequences in inheritance of the fact that a single chromosome contains many genes, and that exchange of genes occurs between the two members of a pair of chromosomes, are taken up in later chapters.

NOTES AND REFERENCES ON CHAPTER 6

The account of the constitution of the chromosomes given in Chapter 6 is based on evidence given in papers by the students of *Drosophila*, particularly T. H. Morgan, C. B. Bridges, A. H. Sturtevant, and H. J. Muller. References to many of the original papers are given in the publications cited in Note 1 of Chapter 1.

THE GENETIC SYSTEM AS A WHOLE

HAVING examined the chief component parts of the genetic system, we proceed to an examination of the way it functions as a whole. This functioning and its consequences constitute what is usually called Heredity.

As we have seen, the genetic system consists mainly of the chromosomes with their genes: the X-chromosomes, the autosomes, and the Y-chromosome.

Why are the other parts of the germ cells not to be considered 'materials of heredity' or parts of the genetic system—the cytoplasm as well as the chromosomes? It is known that the cytoplasm is of the very greatest importance in the development of the individual and in the production of its inherited characteristics. It is in the cytoplasm, through interaction with the genes, that the differentiations of the body arise.

The rôle of the cytoplasm, however, differs from that of the chromosomal materials in the following respects. Different germ cells differ effectively in their genes, and it is to these gene differences that the appearance of diverse characteristics in different individuals is due. But as a rule there is no evidence that the cytoplasm of different germ cells is effectively diverse in such a way as to produce different characteristics in different individuals. It is therefore the former—the chromosomes with their genes—that are commonly classified as the 'materials of heredity'—more properly perhaps the 'materials of hereditary diversity'. The cytoplasm might correspondingly be called the 'materials of bodily differentiation'.

Following the prevailing usage therefore, we may define the genetic system or material of heredity as follows:

The genetic system consists of those parts of the cells that

THE GENETIC SYSTEM AS A WHOLE

are effectively diverse in different germ cells, these diversities causing different characteristics to appear in the different individuals produced.

In rare cases, in certain plants, it is found that the cytoplasm contains colour bodies which may differ in different germ cells and so cause differences in the characteristics of the individuals developed from them. In such cases the cytoplasm, or at least the colour bodies it contains, must be included as part of the genetic system.¹ But in most organisms the genetic system consists of the chromosomes with their genes.

Constitution of the Chromosomes *The Groups of Characters. Linkage*

Each of the chromosomes (save in some cases the Y-chromosome) is composed, as we have seen, of many diverse genes, as represented in the maps of Fig. 38. In the wild, unmodified individuals, in the fruit-fly, the genes are such as produce the 'normal' or 'wild-type' characteristics of the individuals. The genes of any chromosome become modified in the course of time, in the process known as mutation, which will be dealt with in a later chapter. The modified genes produce altered characteristics, most of which are recessive, while the normal characteristics, when mated to the modified characteristics, are dominant. A few of the modified characteristics, however, are dominant when mated with the normal or wild-type characters. The modified characteristics resulting from mutation are in most, if not all, cases defects, as compared with the normal characters. Thus the normal, dominant characters form a standard condition, of which the defective and recessive mutated characters are modifications.

The diverse genes of any chromosome are designated, so far as they have received names, by the name of one of the modified characters which it helps to produce. Thus the gene yellow, near the upper or left end of the X-chromosome of *Drosophila*, produces in its mutated condition the modified

CONSTITUTION OF THE CHROMOSOMES

body colour yellow; while in its unmodified condition it produces the normal grey colour of the wild fly. In the maps of Fig. 38, all the names apply to the modified or mutated condition of the gene. For every such modified gene there is a corresponding unmodified normal or wild-type gene. It is the custom to designate the wild-type gene from which any modified gene is derived by writing with the name or abbreviation for the modified gene the sign +. Thus yellow+ or y+ or +y signifies the normal wild-type gene that produces grey body colour; white+ or w+ signifies the normal gene located at I, 1.5, which produces red eyes in place of white ones.

The genes of any one of the chromosomes, as X, or a given autosome, become modified in many different ways, so that different examples of the same chromosome have different sets of genes. The diversity of genes in the chromosomes of different germ cells causes diversities in development, with resulting different characteristics in the individuals produced. The characteristics produced by the action of the genes of any chromosome follow in the individuals of successive generations the distribution to the offspring of the genes that produce them. Thus many characteristics follow the course of the X-chromosome; many follow each autosome; a few may follow the Y-chromosome.

Since a large group of characteristics follows each chromosome, the result is that characteristics pass from parent to offspring in groups. As an X-chromosome passes from the father into his daughters, all the genes, and all the characteristics that they produce, pass together into the daughters. Here, of course, some of the recessive characteristics may remain hidden in the presence of dominant genes in the second X-chromosome carried by the daughters. But all may reappear anew when in a later generation this X-chromosome is again by itself in a male. Except in so far as there is exchange or crossing-over with the other chromosome of the pair, all the characteristics that depend on the genes of a particular chromosome pass together into the individual that receives that chromosome, and this continues for generation after generation.

THE GENETIC SYSTEM AS A WHOLE

Thus, in *Drosophila*, suppose that a male has white eyes and yellow body, two characteristics connected with genes in the single X-chromosome. He is mated with a female that has red eyes and grey body, again owing to genes in the X-chromosome. In the daughters of these two, the two types of X-chromosomes are present together. These daughters produce offspring in a third generation (see Fig. 32). Some of their sons receive the X-chromosome that came from the original male; these will have white eyes and yellow body. Other sons receive the X-chromosome that came from the original female; these have red eyes and grey body. Only a very minute proportion of the offspring have the reverse combinations of characteristics—white eyes with grey body, and red eyes with yellow body. The two characters originally together—white and yellow—appear to be linked, and the same is true of the other combination, red and grey. The original combinations do not readily separate. Fig. 32 shows a diagram of these relations.

This linkage of characters in heredity was observed before it was known that characteristics depend on chromosomes. Many theories were invented to account for it, until it was discovered that it is due to the fact that the linked characters depend on genes that are in the same chromosome. All characteristics that depend on the same chromosome form what is called a linkage group. Since there are different numbers of chromosomes in different organisms, there are correspondingly different numbers also of linkage groups.

These linkage groups are of great importance in heredity. They reveal to us many things about the nature and action of the genetic system. We shall therefore examine these groups in a typical organism, selecting for this purpose the animal in which they are best known, namely, *Drosophila melanogaster*.

The Groups of Linked Characters in Drosophila

The fruit-fly has, as we have seen, four pairs of chromosomes (Fig. 7). On the genes in these four pairs of chromo-

THE GROUPS OF LINKED CHARACTERS

somes depend several hundred known inherited characteristics. These many characteristics form four linked groups, according to their dependence on genes in the X-chromosome, or in the chromosomes II, III or IV of Fig. 7. It is to be noted that all of the characteristics that depend on genes in either one of a given pair of chromosomes constitute a single linkage group, since all those characteristics may become connected with the genes of a single one of the chromosomes. Thus the number of linkage groups is the same as the number of pairs of chromosomes.

In the course of breeding successive generations, linkage of characteristics shows itself in the fact that certain characteristics (dependent on genes in the same chromosome), which are present together in one parent, are present together also in the individual descendants. This is best seen on comparing grandchildren with grandparents, as is illustrated in Fig. 32. In this case one grandparent had the combination white-yellow, the other the combination red-grey. The same two combinations reappear in the grandchildren (seen particularly in the grandsons). In addition there are a very few 'cross-overs', having the new combinations white-grey in some individuals, red-yellow in others. But almost all the grandchildren get both the characteristics from the same grandparent. If the original grandparents have the other combinations, grey-white and yellow-red, then the majority of the grandchildren show these combinations.

Thus just what combination of characteristics the individual grandchildren have depends on what characteristics were united in the grandparents. But this is the case of course only for characteristics whose genes lie in the same chromosome. If two characteristics depend on genes that are in different pairs of chromosomes, then the combinations that were present in the grandparents are no more frequent in the descendants than are the reverse combinations. The combinations in such a case are those indicated in table 2 on page 120.

It is in many respects most convenient to think of linkage in terms of the gametes. The combination of genes that are

THE GENETIC SYSTEM AS A WHOLE

present in the gametes can often be determined by examination of the offspring produced. With relation to the gametes, linkage can be characterized as follows. When an individual (zygote) is formed by the union of two gametes, each bearing in one of its chromosomes a certain combination of linked genes, this same individual later produces gametes of which

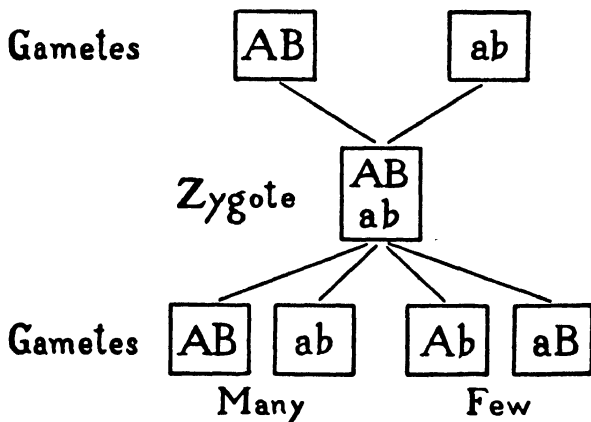


FIG. 39.—*Diagram of the results of linkage, with relation to the gametes. The two gametes above carry respectively the linked genes AB and ab. The zygote produced by their union carries both AB (in one chromosome) and ab (in the other). Then the majority of the gametes formed by this zygote carry again the linked genes AB or ab; only a minority carry Ab or aB.*

the majority have these same combinations of linked genes. Often also there is a minority of gametes that have the genes combined in a new way, as a result of crossing-over. These relations are shown in Fig. 39.

In the fruit-fly, crossing-over occurs only in the females, not in the males. Thus if a male individual is formed by the union of two gametes carrying certain combinations of linked genes, then later such a male produces only gametes having the same combinations of linked genes. This fact is extremely convenient for determining what characteristics are linked in *Drosophila*. There are many other organisms in which crossing-over is not limited to one sex.

THE GROUPS OF LINKED CHARACTERS

By breeding for successive generations and by the study of exchanges between the chromosomes, the following groups of linked characters have been found in the fruit-fly.²

Group I.—A large group of sex-linked characters, more than 100 in number. These all follow in heredity the distribution of X-chromosomes, as described in earlier pages. Any two or more of these characters may be linked together and connected with the same X-chromosome.

Group II.—A large group of typical Mendelian characters, 50 to 100 or more in number. These follow the method of distribution of autosomes, and any two or more of the group may be connected with the same autosome.

Group III.—Another large group of typical Mendelian characters, 50 to 100 or more in number, following the method of distribution of autosomes. Any two or more of this group may be connected with the same autosome, but a character of Group III is not linked with any character of Group II.

Group IV.—A small group of typical Mendelian characters, only 5 or 6 known. These are not linked with any of the characters of Groups I, II or III.

All of the 300 or more characters known in this species fall into one or the other of these four groups. The nature of the characters found in the different groups is considered on later pages.

Thus here the number of linked groups is the same as the number of pairs of chromosomes. There are three large groups and one very small one; likewise there are three large pairs of chromosomes and one very small pair (Fig. 7). It is natural to conclude, therefore, that the groups of linked characters correspond to the pairs of chromosomes, and that the characteristics in each group are connected with some particular pair. As it turns out, there is conclusive evidence that this is true. The evidence for each of the groups may be summarized as follows:

All the characters in Group I are sex-linked; that is, they follow exactly the distribution of the X-chromosomes. Any character in this group follows a particular X-chromosome

and its descendants, wherever that chromosome goes. The characteristics in Group I are thus certainly dependent on genes in the X-chromosomes.

The small group of characters known as Group IV has been proved to be connected with the small chromosomes of pair IV (see Fig. 7). This has been demonstrated in the following manner (see Fig. 40). By non-disjunction of this fourth pair of chromosomes, some individuals are produced having but one small chromosome (IV). That this is the situation can be seen under the microscope, in properly prepared material.

These individuals with but one of the small chromosomes have the dominant normal or 'wild' characteristics. Such individuals are mated with individuals containing one of the recessive characters of Group IV (Fig. 40). One of these recessive characters is 'bent wings'; another is 'eyeless'—the individual having no eyes.

Half of the germ cells from the individuals that have but one of the fourth chromosomes are without this chromosome, while half of them have it. These two kinds each unite with germ cells carrying the recessive character 'bent', or 'eyeless'. There are thus produced individuals, half of which have but one of the fourth chromosomes, while the other half have two (Fig. 40). In those which contain two, all the characteristics are of the dominant normal type; the recessive character bent or eyeless is not manifested. But in the individuals having but one fourth chromosome, the recessive character is manifested: the individual shows bent wings, or is eyeless. This demonstrates that the characteristics of Group IV are connected with the small chromosomes.

Thus the large linkage Groups II and III are left for the two large V-shaped chromosome pairs, II and III. These chromosomes can be broken into two or more pieces by subjecting them to radiations. When this is done, the characters of the corresponding linkage groups are no longer linked together. Thus in Group III the two genes *scarlet* and *sooty* are linked (completely in the male). But when the corresponding large chromosome (III) is broken into two pieces, scarlet and sooty are no longer linked; they may pass to different offspring.

THE GROUPS OF LINKED CHARACTERS

They are evidently connected with the two separated pieces of chromosome III. In the same way the other large chromosome (II) may be broken, and this causes the characteristics of the linkage Group II to separate into two groups. Minute

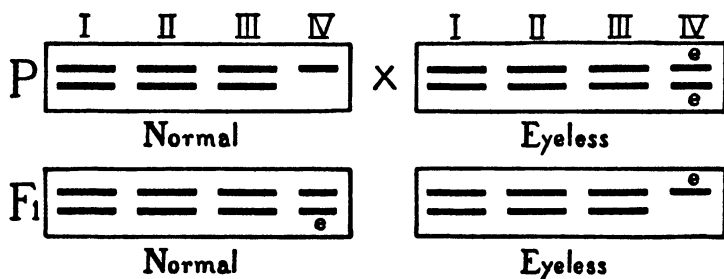


FIG. 40.—Diagram of the mating that shows that the recessive character *eyeless* (*e*) is dependent on a gene in chromosome IV. Of the two parents, one, having but one chromosome IV, has normal eyes; the other is eyeless. Forming germ cells and mating them in the usual way, two types of offspring are produced in *F*₁. One type, with two of the fourth chromosomes, is normal; the other, with but a single fourth chromosome, is eyeless, thus proving that the gene for eyeless is in chromosome IV. For if *e* were in one of the other chromosomes, the presence of a normal member of the pair would prevent the manifestation of the recessive eyeless.

study shows that the chromosomes II and III differ a little, in size and form, so that with practice it becomes possible to distinguish one from the other under the microscope.

Thus it is proved that each of the four linkage groups is connected with one of the four chromosome pairs; the four groups correspond to the four chromosomes.

In a number of other organisms the number of linked groups of characters has been determined, and also the number of pairs of chromosomes. In every case in which this has been fully worked out, the number of linked groups is the same as the number of pairs of chromosomes. The numbers of groups and of pairs in certain organisms are as follows:

Drosophila melanogaster 4, *Drosophila virilis* 6, garden pea 8, sweet pea 8, maize 10.

THE GENETIC SYSTEM AS A WHOLE

In man there are twenty-four pairs of chromosomes, including the X's. It is to be expected therefore that there will be found 24 groups of linked characters, one group sex-linked, the other 23 groups typical Mendelian, in their inheritance. But it will be a very long time before these 24 groups are identified.

What kinds of Characteristics are found in the different Linked Groups? Functions of the different Chromosomes in their Relations to Characteristics

Have the different chromosomes different functions? Can we classify their functions in any simple or systematic way? Do certain chromosomes influence certain particular parts of the body, or certain particular functions, while others influence other parts or functions?

Such questions can be answered by an examination of the kinds of characteristics found in each of the linked groups; this will show what kinds of characteristics are influenced by each of the chromosomes. We give, therefore, the following lists of a number of typical characteristics connected with each chromosome in the fruit-fly. The characteristics listed are all modifications of the normal characteristics found in the typical wild fly. Hence for every characteristic here listed there exists also a corresponding unmodified normal characteristic. Each of the characters listed is the result of modification of a single gene.

List of some Typical Characters connected with the Genes of each of the Four Chromosomes of the Fruit-fly

In the lists, the part of the body, or the function, affected by the character is first indicated. This is followed by the names that have been applied to the different characteristics. Many of these are self-explanatory; of some others a brief characterization is given.

Group I.—X-chromosome. Sex-linked inheritance. Eye-

CHARACTERS CONNECTED WITH THE GENES

colour: coral, blood, eosin, cherry, apricot, buff, tinged, ivory, white (the foregoing are multiple alleles; that is, they are all diverse modifications of the same gene). Modifications of other genes: vermilion, ruby, carmine, garnet.

Eye form or structure: bar, facet, furrowed.

Body colours or markings: yellow, sable, lemon, green, chrome, tan, spot, dot, etc.

Wings: rudimentary, miniature, bifid, bow, notch, depressed, club, fused, cut, etc.

Legs: reduplicated.

Body structure: abnormal abdomen.

Bristles: forked, singed, tiny, bobbed, scute.

Reactions to light: tan (individuals showing this colour characteristic do not fly toward the source of light, as do the normal individuals).

Life and health: at least 10 different lethal genes are known to be connected with the X-chromosome. Any one of these prevents the animal from developing, if no corresponding normal gene of the same pair is present. All, or practically all, the characteristics in the above list cause the organism showing them to be weaker and less resistant than the normal 'wild-type' flies.

As will be seen from the above list, the genes of the X-chromosome affect practically all parts of the body, and many of its functions.

Group II.—Second chromosome (autosome). Mendelian inheritance.

Eye colour or structure: purple, pinkish, cream, star, morula, etc.

Body colour and pattern: olive, black, streak (thorax), comma, trefoil, speck, patched abdomen, etc.

Wings: truncate, balloon, vestigial, blistered, jaunty, curved, strap, apterous (and many others).

Bristles: fringed, minute, vortex.

Life and health: lethals (several).

Thus chromosome II affects many parts of the body.

Group III.—Third chromosome (autosome). Mendelian inheritance.

THE GENETIC SYSTEM AS A WHOLE

Eye colour or structure: claret, cream III, deformed, kidney, maroon, pink, peach, rough, scarlet, sepia, etc.

Body colour or pattern: band (thorax), ebony, sooty, trident, etc.

Body structure: bithorax, dwarf, giant.

Wings: beaded, spread, tilt, truncated, etc.

Bristles: doubled, hairless, hairy, minute, spineless, two-bristle, vortex III, etc.

Life and health: several lethals.

Thus chromosome III also affects many parts and functions.

Group IV.—Fourth chromosome (autosome). Mendelian inheritance.

Eyes: eyeless.

Wings: bent; cubitus interruptus.

Bristles: shaven.

Few genes known, but affecting diverse parts of the body.

What does the foregoing list of characters affected by the different chromosomes show as to the nature and functions of the chromosomes?

1. All the large chromosomes (Nos. I, II, and III) affect all parts of the body: many different functions, health, length of life, and the like.

The small pair (IV), though affecting few characters, still affects diverse parts (eyes, wings, bristles).

2. Thus particular chromosomes are not limited in their action to any particular part of the body or to any particular function. Each chromosome affects many parts and functions.

3. It appears clear that each chromosome enters into the process of development, affecting many processes, and doubtless influencing the entire organism. The method of action of the X-chromosome has been treated in a previous chapter; as there seen, it alters the chemical processes, thus affecting the development of all parts of the body. The other chromosomes doubtless act in a somewhat similar manner.

4. It is not clear from our present knowledge that the genes are arranged in the chromosomes in any systematic way, with

CHARACTERS CONNECTED WITH THE GENES

relation to their functions, or to the parts of the body that they chiefly influence. A gene principally affecting eye colour is close to one principally affecting body structure or body colour or structure of the wings, and so on (see the maps, Fig. 38). Genes affecting eye colour occur in many different parts of the genetic system. In Fig. 41 (next chapter) are shown sketch maps of the three large chromosomes, indicating the position of 19 genes that are known to influence eye colour. In a similar way, genes that affect the structure of the wing or of the eye, or that affect the colour of the body, are scattered throughout the four chromosomes.

Thus if there is any functional system in the arrangement of the genes in the chromosomes, it has not yet been discovered; in the present state of our knowledge it appears as if there were none.

NOTES AND REFERENCES ON CHAPTER 7

1. Page 162. On the relation of the cytoplasm to inheritance, see the recent review by E. M. East (1934), 'The Nucleus-Plasma Problem', *The American Naturalist*, vol. 68, pp. 289-303, and 402-439.

2. Page 167. For the groups of linked characters in *Drosophila*, as well as other matters connected with the genetics of this animal, see the publications referred to in Note 1, Chapter 1.

8

RELATION OF GENES TO CHARACTERISTICS

By 'characteristics' or 'characters' are meant any features, physical, chemical, physiological, or structural, in which organisms may differ. The materials presented in the chapters preceding this one have brought out, explicitly or implicitly, many of the relations between genes and characteristics. Here these relations, and others not yet set forth, are brought together in systematic order.

1. *Special Action of a Gene.*—Particular genes affect mainly, though not exclusively, some particular part of the body, or some particular function.

Thus, in *Drosophila* there is in the X-chromosome, at the locus I, 1.5, a certain gene which in its normal condition takes part in producing the red eye colour. This gene has become modified in different cases in a considerable number of different ways, and any modification alters the colour of the eye. The different modifications give the many different alleles listed in Chapter 7 among the eye-colour characters of linkage Group I. Other genes have their chief effect on the body colour or on the wings or on some other part. Particular genes in man affect the blood type of the individual; others affect the eye, the body form, and so on. Each gene as a rule has its main function in connection with the development of some particular part.

2. Yet a given gene often produces effects on several parts or functions. For modification of a single gene may cause a change in the characteristics of a number of different parts. Some examples of this may be given.

The character *bent wings*, belonging to linkage Group IV of *Drosophila*, is due to the modification of a single gene in chro-

SPECIAL ACTION OF A GENE

mosome IV. It causes the wings to be bent dorsally at their base, and also it causes the legs to be shorter than normal, owing to the abnormal shortness and thickness of the metatarsal joint.

In animals showing the character *vestigial wings* (due to modification of a gene in chromosome II), the following peculiarities appear: the wings are degenerate, only their bases being present, and these are held at right angles to the body. The balancers are likewise degenerate. Two rear bristles on the scutellum are farther apart than usual, and they stand up straight instead of inclining backward. The flies hatch about two days later than in the normal wild flies. They are not quite so vigorous as the normals.

As noted in the preceding chapter in connection with linkage Group I, modification of a certain gene in the X-chromosome causes (1) the body colour to be tan instead of grey, and (2) causes the individuals to lose the usual positive reaction to light.

In any detailed account of the effects of particular genes, it will usually be found that each gene has thus several different effects, often on diverse parts of the body. The effect on which the name given to the gene is based is commonly merely that effect that is most conspicuous to the eye.

3. *General or Constitutional Effect of a Gene.*—In addition to the special effects on certain structures or functions, modification of any gene has also a general effect on the bodily constitution. In *Drosophila* the 'wild-type' flies, with unmodified genes, are vigorous and long-lived. Practically all modifications of the normal genes make the animals less vigorous, so that individuals showing any of the characteristics listed in the preceding chapter are weaker than the normal or 'wild-type' individuals, and have a higher rate of mortality. Thus practically all the modifications of normal genes are defects, a fact to which we return in a later chapter.

In view of the facts set forth in preceding paragraphs it has been said with much probability that 'every gene affects the development of the entire body'.

4. Thus apparently each gene supplies material which in

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the process of development enters into reaction with materials from all the other genes; it thus modifies many or all parts of the body, but affects certain parts more conspicuously than others.

5. As before set forth, a particular single gene may become modified in many different ways, in different individuals or different chromosomes, each modification causing a changed characteristic. The classical example of this is the series of different eye colours (multiple alleles) found in different individuals of *Drosophila*, each colour being due to a different modification of the gene located at the point I, 1.5 in the X-chromosome. This gene in its normal condition produces (by interaction with other eye-colour genes) the normal red colour. The various modifications of the gene give rise to the colours before mentioned: coral, blood, eosin, cherry, apricot, buff, tinged, ivory, white.

Many such series of multiple alleles are known in the fruit-fly and in other organisms. In the fruit-fly the following illustrate their nature:

Scute: The gene scute is close to the upper (or left) end of the X-chromosome. It exists in 20 to 30 different modifications, each of which causes a slight change in the distribution of the bristles on the body.

Cut: A considerable number of different alleles are known of the *cut* gene, located at I, 20.0. All of them cause changes in the outline of the wings, as if bits of the wing were cut off.

Vestigial: The gene vestigial at II, 67, which reduces the size and changes the form of the wing, has two other alleles, *antlered* and *strap*, giving wings of other forms and sizes.

Garnet: At the locus I, 44.4 are several alleles which change the colour of the eye in diverse ways. Some of these are known as garnet, salmon, garnet 2, garnet 3.

Pink: The eye colours, pink, peach, pink 3, pink 4, pink 5, are a series of alleles located at III, 48.0.

Series of alleles are known also in other organisms. Thus in the rodents (rats, guineapigs, rabbits), series of different alleles are known, yielding different colours of the hairy coat. In maize there are several allelic series modifying the colour

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of parts of the plant. Presumably any gene may, by successive modifications, produce a series of alleles.

As mentioned in an earlier chapter, all the members of an allelic series affect the same character or part of the body, yielding different modifications of that character. Further, they show certain peculiarities of inheritance as compared with different genes that are not alleles. Since they are all modifications of the same gene, only one of the alleles can be present in a single chromosome, and for this reason only one of them can be carried by a single gamete (except in cases of non-disjunction). Further, only two members of a given allelic series can be present in any diploid individual or zygote.

There are thus two types of diversities among genes. (1) On the one hand, there are the different genes occurring at different loci in the chromosomes, the diverse genes, shown on the maps (Fig. 38), affecting many diverse characteristics. (2) On the other hand, there are these different modifications of a single one of these genes—the multiple alleles.

6. Any given single character, inherited in the sex-linked or the autosomal manner, is a product of the interaction of many genes, located in different parts of the genetic system.

As an example of this, the colour of the eye in *Drosophila* may be taken. As shown in the preceding chapter, the colour of the eye depends on many genes scattered through the different chromosomes. Fig. 41 is a diagram of the chromosomes, showing the location of nineteen different genes that affect the eye colour. The number of different genes directly affecting the colour of the eye is indeed still greater than this, and in addition there are many other genes that affect eye colour indirectly, through the fact that they affect the structure of the eye: for example, the gene 'eyeless' in the fourth chromosome pair. If this gene is modified in a certain way, no eyes are developed, consequently no colour.

Similarly, many different genes affect the form and structure of the wings, the venation of the wings, the structure of the eye, the colour of the body, the form of the body, the structure and distribution of the bristles. Indeed, this is

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presumably the situation with relation to any characteristic whatever; every characteristic is influenced by many genes.

7. Altering any one of the numerous genes that cooperate to produce a given characteristic alters that characteristic. Any characteristic may, therefore, be changed by altering any one or more of many different genes.

Thus, consider what must be the situation among the genes to yield the normal red eye colour in *Drosophila*. To produce this result all of the 19 (and more) genes that affect eye colour (Fig. 41) must be present in the usual or normal condition. If any one of them is changed (the rest remaining unchanged), the colour of the eye is altered.

Changing in a certain way a gene at I, 1.5 (see maps, Fig. 38), all other genes remaining normal, the eye colour is changed to white. If we change the gene at I, 33 (the rest remaining normal), the colour becomes vermillion. If we change the gene at II, 54.5 (the rest remaining normal), the colour of the eye becomes purple. Thus one could go over the entire 19 genes; changing one after the other; each one changed alters the eye colour.

Again, consider what must be the situation in the genetic system to yield one of the recessive colours: for example, vermillion eye colour. To produce this colour, 18 of the genes must be in their usual normal condition, while a single one, at the point I, 33, must be altered. If, in addition to this one, another is altered (for example that which by itself yields purple, at II, 54.5), a different colour is produced. Altering one gene changes the colour in a certain way; altering two or more changes the colour in a still different way. Similar relations would be found with respect to most or all characteristics.

8. '*Multiple Factors*'.—The different genes on which a given character depends may have qualitatively different effects; such is the case with the different genes that affect the eye colour in the fruit-fly. In other cases the different genes affect the characteristic only quantitatively. Thus dimensions often depend on many different genes. Modifying one of these or substituting another for it changes the dimension; modifying

SPECIAL ACTION OF A GENE

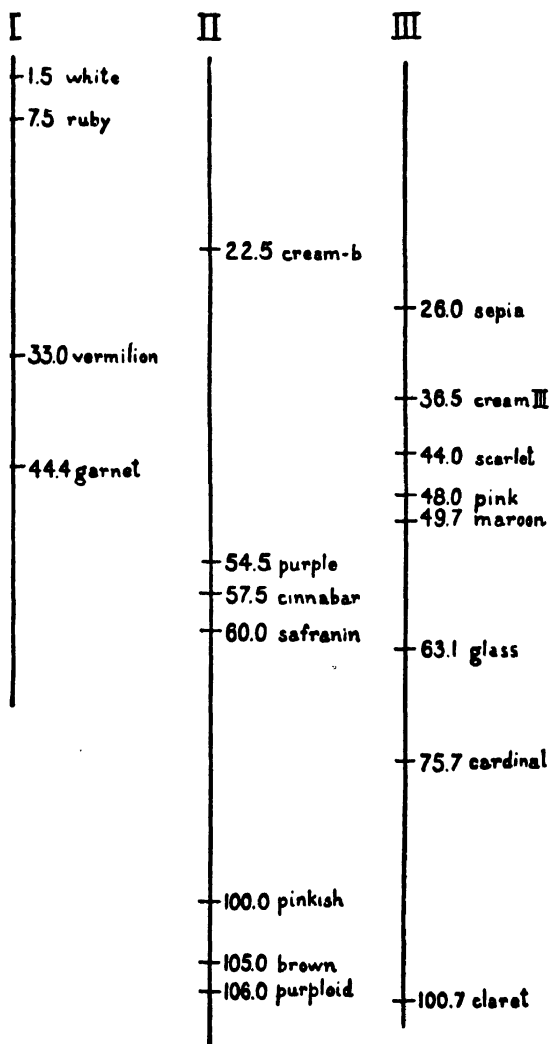


FIG. 41.—Sketch map of the three large chromosomes of *Drosophila melanogaster*, showing nineteen diverse parts (genes) of the genetic system that cooperate in development to produce the eye colour. The numbers before the names are the locations of the respective genes, in unit distances from the upper ends of the chromosome.

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an additional one changes it still more, and so on. In such cases the character is commonly said to depend on 'multiple factors'.

9. '*Duplicate Factors*'.—In some cases a character may depend on the presence of two (or more) genes of a particular type in such a way that both of these genes must be present in order that the character shall be produced. The character is then said to depend on duplicate genes or factors. In the plant known as the shepherd's purse, the common type of pod is triangular, but some plants have an elongated oval pod. This oval pod occurs only when two particular recessive genes are present in the homozygous condition. Thus if the two dominant genes which produce the triangular pod are A and B, while the two recessives that give the oval pod are a and b, the oval pod occurs only in the plants having the genes aabb, while all the other combinations of table 2 on page 120 give the triangular pod.¹ Similar cases of duplicate genes are known in a number of organisms.

10. '*Modifying Factors*'.—In some cases the effect of some of the genes is merely to modify in detail a characteristic that is due primarily to another gene. Such are known as modifying genes or factors. Thus, in *Drosophila*, a certain modified gene at I, 1.5 causes the eye to assume the pinkish colour known as eosin, but the depth of this eosin colour depends upon certain other genes present in other parts of the genetic system. One of these, known as cream b, is located at II, 22.5; another, cream III, at III, 36.5; and several other such genes modifying the eosin colour are known. If these genes are present in the normal or unmodified condition they do not affect the eosin colour; when modified in certain ways they do. Again, in the rat, the presence of a certain gene causes the fore part of the body to be coloured brown, forming what is called a *hood*, the rest of the body being white. The extent of this hood depends on the presence in the individual of a number of other genes; some of them increase its extent, others decrease it.² Such modifying genes or 'modifying factors' play a rôle in many characteristics. They may produce no visible effect except in the presence of a particular character that they

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modify. Thus the modifiers of eosin eye colour produce no visible effect in an individual with red eyes.

11. The same phaenotypic character—that is, the same characteristic in outward appearance—may be due in different cases to the alteration of diverse genes, in different parts of the genetic system. This is illustrated in numerous cases in *Drosophila*.

Thus, modification of a certain gene at II, 54.5 causes the colour of the eye to change from the usual red to a darkish purple; the modified gene giving this colour is known as purple. But in other cases what is outwardly the same colour is found to be produced by change in other genes. One of these is at I, 44.4; to distinguish it from the one just mentioned it is called garnet. A third gene that produces practically the same eye colour is found at III, 49.7; it is called maroon.

Similarly the eye colour 'salmon', resulting from a modified gene at I (again at 44.4), is indistinguishable from the eye colour 'rose', resulting from a gene modification at III, 48.0.

Other cases of this sort could be given. In such cases the same phaenotypic character will be found to be inherited in different ways in different cases, depending on the location of the modified gene to which the character is due. If the gene is in X, the inheritance will show itself to be of the sex-linked type; if in II, it will be autosomal and of the linkage Group II; if in III, it will be autosomal and of the linkage Group III (see Chapter 9, on Rules and Ratios of Inheritance).

The Action of Genes in Development

In view of what has just been set forth, how are we to conceive the operation of the genes in producing the characteristics? How do they operate in producing an adult from the fertilized egg? And how do different sets of genes produce individuals having different characteristics?

On the intimate details of the operation of the genes little is known. Some of the main features in their method of action were taken up in Chapter 3, in dealing with the relation of

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chromosomes to sex, though only the action of large groups, forming chromosomes, was there dealt with. From the relations brought out above, and in preceding chapters, taken in connection with the facts of embryological development, it is possible to form a conception of some of the main features in the action of genes in building up the body. These are summarized in the following.

The genes form a set of many diverse materials, differing from each other chemically and physically and having different chemical and physiological activities. They exist at the beginning of the individual's development in the nucleus of the fertilized egg, while surrounding them is a mass of cytoplasm.

The genes interact with the cytoplasm, changing it, producing new materials that are incorporated into the cytoplasm. These varied cytoplasmic products of the different genes interact with each other, producing again new types of material.

Some of the gross features of the interaction of genes and cytoplasm were described in Chapters 2 and 3 (see Fig. 15, page 53). As there shown, the chromosomes (groups of genes) visibly take up material from the cytoplasm, alter it, and give it off again into the cytoplasm.

Though the genes thus interact with the cytoplasm, modifying it, they are not themselves used up in this process so as to lose their essential character. They supply material which combines with cytoplasmic material. But there is left an unchanged part of each gene, and this by division produces additional genes of the same type and action.

As the cells divide, each chromosome divides, and each of its contained genes divides. One of the two halves of each gene goes after division to each of two cells produced. Thus each new cell produced contains the full set of genes, all those that were present in the fertilized egg.

In most organisms it appears probable that this continues throughout at least all the early stages of development, if not to the end of development, so that all the cells contain all of the genes. For in the young embryo, after many hundred cells have been produced, it can be shown that any cell can

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produce many different parts of the organism. And in many organisms even in late stages there are cells that can produce any part, or the whole organism, as is shown by the facts of regeneration. Such cells must contain the entire set of genes.

In very late stages of development it is possible that in highly differentiated tissue cells some or all of the genes have

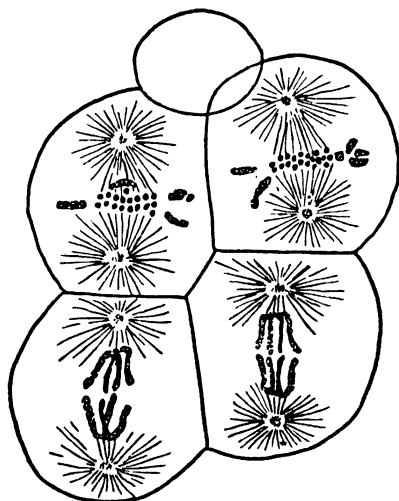


FIG. 42.—*Dividing cells of an early developmental stage of Ascaris megalocephala, after Boveri (1910). The chromosomes in the two large upper cells are broken into fragments, part of which are dissolved and lost, while in the two lower cells the large chromosomes remain entire.*

become lost or modified, though there is no clear proof of this. Further, there are a few organisms of which it is to be observed that the cells that are to produce the differentiated body of the animal lose parts of their chromosomes, and so presumably some of the genes. The chromosomes in these cells are seen to break up, and portions of them are dissolved and absorbed by the cytoplasm (Fig. 42), while in the germ cells the chromosomes remain entire. This is known to occur in threadworms (Nematodes) and in certain insects. The relation of these processes to the way bodily development occurs is quite unknown.

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But on the whole the evidence is strong that in most organisms the production of different tissues and organs by different cells is not due to their containing different genes, for cells that certainly contain all the genes produce many different parts in many different cases. The genes act differently in the different cells, depending on the relation of the different cells to each other, so that the different cells, though containing the same genes, produce different tissues and organs (see Chapter 10 for experimental evidence as to this).

The diversity of the different parts of the body seemingly arises mainly, if not entirely, through the fact that different cytoplasmic products of the genes are separated into the different cells. Thus the cells become different in their cytoplasm. And this different cytoplasmic constitution of the different cells interacts differently in each case with the full set of genes that the nucleus contains, so giving anew different products. By a continuation of such action the different tissues and organs are produced. In each, the cells contain the same sets of genes, but differ in their cytoplasm. The differentiations of the body therefore lie mainly in the cytoplasm, though the diversities in the cytoplasm are brought into existence through the action of the genes.

Yet it is true that differences may arise within the body of a single individual through a change in the genes of some of the cells. As before seen (Chapter 3), if in a female *Drosophila* one of the cells loses one of the X-chromosomes, that part of the body derived from this cell shows the characteristics of the male, while the rest is female. If the X that is lost carries dominant genes, while the remaining X has the corresponding recessive genes, then, in that part of the body whose cells have lost one X-chromosome, the recessive characters are manifested, while the remainder of the body is dominant. In this way are produced mosaic organisms, showing diverse hereditary characteristics in different parts of the body. Such mosaic diversities, however, appear to be of a very different type from the differentiation of the body into tissues and organs. Whether any differentiations in ordinary development are thus produced through loss or modifications of

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certain genes must be considered as yet uncertain, though it is entirely clear that most of them are not so produced.

But diversities between individuals, as we have seen, commonly result from differences in the genes that they contain. If two fertilized eggs begin with different sets of genes, the processes of changing the cytoplasm, of differentiating it into tissues and organs, differ in the two cases, so that individuals with diverse characteristics are produced. Very marked differences in characteristics may be produced even when the two sets of genes differ in but a single gene or pair of genes. In *Drosophila*, as before seen, if two eggs differ in a single pair of genes in chromosome IV, one of them produces individuals without eyes, while the other has normal eyes. If two individuals differ in an entire chromosome (X), one becomes a male, the other a female.

Such differences are due to the diverse chemical and physical action of the different genes. They produce differences among different cells, in the way set forth in earlier paragraphs. Also, they may produce diverse chemicals (hormones) which circulate through the body, in the way described in Chapter 3, thus causing changes in the development of parts with which they come in contact.

Different chemical and physiological effects, different development, may be produced by difference in balance among the genes, as shown in Chapter 3. Two cells may contain the same kinds of materials (genes) throughout, but one of these contains certain materials in two *doses* (a pair of genes), while the other contains but one dose (an unpaired gene). In consequence the two cells differ greatly in development. In this way difference in sex is produced, with its manifold attendant differences in structures and functions. In many cases two genes of a certain kind produce a different effect from a single one, though in other cases they do not. That is, two centres of a certain kind of action may give different results from a single centre. This principle of the effects of difference in balance is presumably of great importance, though as yet not a very great deal is known as to its operation.

It appears possible that the operation of some or all of the

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genes begins in early stages of development and continues throughout. It is known that some genes produce their distinctive effects at the beginning of development, in the egg itself. Thus in the silkworm a difference of one gene is known to make a difference in the colour of the egg. Two races differ in egg colour, one having slate-coloured eggs, the other brown eggs. Crossing the two races shows that the difference in colour is due to a difference in a single gene, for the descendants show 'unit difference' inheritance. If, by crossing, the special gene from the slate-coloured race is brought into the eggs of the brown race, in the next generation the eggs are slate-coloured instead of brown, so that the 'slate' gene is active in the formation of the egg.

Other genes are known to produce their distinctive effects somewhat later, but still rather early in development. Thus in mice, if one of the genes of a certain pair is modified in a certain way, this causes the hair of the individual to be yellow. If both the genes of this pair are so modified as to produce the yellow colour, the individual develops for but a short time, then dies while still an embryo. It is clear that these genes are active in the young embryo. Again, in plants, certain genes are required for the production of chlorophyll. If one of these becomes defective, chlorophyll is not produced. The young plant grows so long as the stored food in the seed is available, but, having no chlorophyll, it cannot make use of the sun's rays for the elaboration of nutrition; it therefore dies as a young seedling. Examples of the operation of genes during early development are abundant.

Some genes are required for laying the foundation of certain parts or organs; if these genes are altered, no such organ is produced. Thus in the fruit-fly a certain gene in chromosome IV is necessary, in its normal condition, for producing eyes. If that gene becomes defective, the eyes are completely lacking, although all the other genes that cooperate to produce the eye may be present in normal condition. This particular gene is required for the very foundations of the eye. Similarly, in vertebrates a certain gene is required for the production of the pigment which produces the colours of hair

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and skin. Many different genes cooperate to produce this pigment; most of them modify the type of pigment produced. But if this particular one becomes defective in a certain way, no pigment is produced; the animal is an albino.

A somewhat similar situation appears to be at the basis of some cases of feeble-mindedness in man. In such cases the brain is not properly constituted; it does not function well. Study of inheritance shows that in some cases, at least, feeble-mindedness is due to a defect in a single gene; there is 'unit difference' inheritance. This single gene plays a necessary part in producing an efficient brain; when the gene is defective the brain is fundamentally imperfect.

The special and distinctive functions of some genes are not known to come into operation until late stages of development. Such, for example, are those that produce in *Drosophila* the distinctive pigments of the eye. Their visible effect does not appear until the eye is formed; although of course this action may have begun early in development.

In many such cases in which the conspicuous effect of a gene appears at a relatively late stage in development there are less conspicuous effects that indicate that the gene may be in operation throughout development. Thus individuals with white eyes, or with rudimentary or vestigial wings, are less vigorous than those with normal eyes or wings; they are less resistant and have shorter lives, and this is true for most of the types having recessive characters. Though the conspicuous special effect of the changed gene is late in appearing, the effect on the general constitution indicates that there may be an effect throughout development.

That this is indeed the case is indicated strongly by certain other facts. Sometimes a gene at a certain locus in the chromosome becomes entirely inoperative; it has either dropped out of the chromosome, or it has totally lost its action. Such cases are commonly known as deficiencies. Deficiencies are producible by the action of radiation on the chromosomes, so that large numbers of them have been studied. A deficiency is detected in the following manner. A chromosome suspected of being deficient for a certain gene at a certain

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locus is brought into an individual in which the other member of the pair to which it belongs carries a recessive gene at that locus (Fig. 43). If the chromosome is deficient in the suspected gene, the recessive gene is manifested, since there is present no dominant gene of that pair. Thus if an X-chromosome carrying white eye is brought into a female whose other X is deficient for the gene at the white eye locus (the locus 1.5), the female has white eyes.

In the case of almost any gene, if two chromosomes that are deficient for the same single gene are brought into the same fertilized egg, so that the egg lacks that gene entirely, the egg

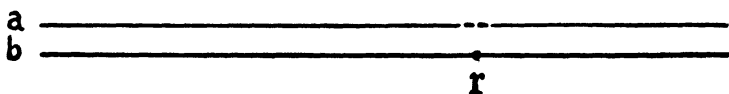


FIG. 43.—*Method of testing for a deficiency. The chromosome *b*, carrying the recessive gene *r*, is brought into the same fertilized egg with the chromosome *a*, which does not carry the recessive. If the recessive *r* is manifested in the individual developed from the egg, this shows that the chromosome *a* has a deficiency at the region *r*.*

does not fully develop. In most cases it is not known at just what stage development ceases. But the fact shows that, in addition to its special effect on a particular characteristic, the gene is necessary if development is to continue at all beyond a certain stage. By ingenious methods Demerec³ has recently proved that if only a few of the cells of a developing embryo are deficient for a certain gene, those few cells fail to develop, though the rest of the body does develop. This was demonstrated for deficiencies of many different genes in the X-chromosome of *Drosophila*. In only one of the many cases tested was deficiency for a certain part found not to be lethal, though even in this case it caused weakness. In the case of the white eye gene at I, 1.5, and in many other loci, deficiency prevented development.

Altogether, it is clear that genes are active throughout development, some beginning early, others seemingly later, and that almost all genes are necessary in order that full develop-

ment shall occur. Changing one or more genes may cause from the beginning a change in the chemistry and physiology of the organism, altering its course of development and so giving rise to changed characteristics.

What kinds of Characteristics are affected by Genes?

The question as to what kinds of characteristics are affected by genes has been much discussed. Some have supposed that only a few characteristics depend on genes: only certain superficial matters, such as colours, and the forms of external features. Particularly with relation to man has there been dispute on this matter.

But on this question, positive knowledge is available, both for man and for other organisms. It is possible to answer fully the question: What kinds of characteristics are affected by genes?

The question can mean only: What kinds of characteristics can be altered by changing the genes? What kinds of differences in characteristics result from differences in genes?

There are several ways of answering these questions. The most direct is by the crossing of individuals having different genes. This results in substituting one type of gene for another, with consequent differences in characteristics. If the diversities in characteristics show Mendelian or sex-linked inheritance, this demonstrates, as we have seen, that they are due to differences in genes.

By this test, in many organisms (for example *Drosophila*), the following kinds of characters have been found to be affected by genes:

(A) Structures and forms of all parts (head, eyes, thorax, abdomen, wings, legs, internal organs).

(B) Colours and patterns of all parts. These depend on chemical processes, hence:

(C) Chemical processes of many kinds are affected by genes.

(D) Physiological conditions: health, vigour, life and death.

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(*E*) Power of development: certain lethal genes stop development at a certain stage. A defective gene in the fourth chromosome of *Drosophila* prevents the development of the eye. Certain genes cause the body to grow to a larger size than usual. Many examples of the effects of particular genes on development have been given in earlier pages.

(*F*) Behaviour. Reactions to light in *Drosophila* are changed by alteration of a certain gene ('tan').

(*G*) Sex. Changing the genes changes the sex; this involves changes in all types of characteristics: in structure, pattern, colour, physiology, behaviour.

Thus, in sum, it is clear that in animals, characteristics of all kinds, without exception, are affected by genes. There are no characteristics that are exempt from influence by the genes. Any characteristic can be altered by suitable alteration of genes. This is not surprising when it is considered that the genes are among the materials from which organisms are made, and that altering them alters the chemistry of the developmental processes.

What is the situation in Man? What characteristics are affected by genes in Man?

In man we have to deal with certain important types of characteristics that are hardly to be studied in other organisms. These are what we call mental characteristics: emotions, temperament, skill, character, intelligence, reasoning power, and the like. There are great differences among human beings in their mental characteristics, and in their capabilities. Are these things affected by genes? Often it is argued that they are not. Some have held that practically all differences in mind and character are due to environment, to education, influence of associates, tradition, state of civilization, and the like.

On this matter there is positive knowledge which completely removes the matter from doubt. There are two methods by which it can be determined in man what kinds of characteristics depend on genes.

1. The first method is by observing what characteristics

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show Mendelian or sex-linked inheritance. This method is not entirely satisfactory in man, since (*a*) it is not possible to carry on experimental breeding in man, and (*b*) this method can hardly be applied to the important mental characteristics. Yet by this method many characteristics of man have been shown to depend on genes. Among the characteristics showing sex-linked or Mendelian inheritance, and so depending on genes, are the following in man:⁴

Colour of hair and eyes; form of many facial features; structure of the hands and feet; form of the body, whether stout or slender; chemical constitution of the blood; efficiency of the brain (whether the individual is normal or feeble-minded); condition of the eyes and sense of sight (colour-blindness, short-sight, night-blindness and other conditions); sense of hearing (deafness, etc.); sex, and many other characteristics.

2. A second method gives much fuller and more detailed knowledge of what characters are affected by genes in man. This is by the study of identical twins, as compared with other individuals. This is a most important method, and it will therefore be discussed in some detail. It depends on the following facts:

(*a*) In man, most individuals are derived from separate germ cells, and therefore have diverse sets of genes. For in forming germ cells, as before described, reduction of chromosomes and genes occurs, so that practically every germ cell differs in its gene combination from every other. When by fertilization two different germ cells unite, the diversity of gene combination is increased still more. The result is that no two individuals formed in this way have the same combination of genes.

(*b*) But rarely there occur cases in which a single fertilized egg produces two individuals (twins). Such individuals are formed by division of all the genes, so that the two twins contain the same gene combination. These are the twins known as monozygotic or identical twins. In another type of twins, the two are derived from separate eggs; such dizygotic twins have diverse gene combinations.

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By comparing the similarities and differences of identical twins with those in other individuals, and particularly with those of twins of the other type, it is possible to find out what characteristics are affected (1) by having all the genes alike, (2) by having different combinations of genes.

'Identical twins', or offspring all having the same genes, occur in many organisms. In lower animals (Protozoa, plants, Hydra, worms, etc.), a single individual often divides into two or more, by 'vegetative' reproduction. All these individuals have the same sets of genes, since in vegetative reproduction every chromosome and every gene divides. Such individuals are very exactly alike. They have been studied a great deal. In such a Protozoan as Paramecium, a great number of individuals are produced in this way, all closely alike. But when conjugation takes place, this gives new gene combinations, and the individuals after they have conjugated are very different.

In one of the vertebrates, the armadillo, identical twins are formed in essentially the same way that they are in man, but are formed regularly.⁵ A single fertilized egg, after developing some distance, divides into four, so that four 'identical twins', or quadruplets, are produced at each birth. The four are extraordinarily alike even in fine details. But twins belonging to different sets (and so having different gene combinations) are often very different.

Identical Twins in Man

Identical twins are produced in man by the division of a single egg into two, so that they may be called monozygotic or 'one-egg' twins. There occur also dizygotic or 'two-egg' twins, produced from two separately fertilized eggs; these are often called fraternal twins. Methods have been discovered by which it is possible to determine to which class any pair of twins belongs.⁶

Identical twins in man are of enormous interest; they supply exactly what is required for discovering what characteristics depend on genes. They are two individuals that are

made throughout from the same set of materials, from the same set of genes. Every single gene of one has its exact duplicate in the other. The two therefore have the same heredity; the differences between them are due to environment alone. They show how like or how diverse will be two human beings that do not differ in their genes, in their heredity, although they may differ in the conditions of their lives, in the experiences they undergo. Identical twins thus form one of the most interesting and illuminating of the phenomena that nature presents to us. They yield the key to that ancient question, the relative rôle of nature and nurture: of heredity and environment.

The existence of the two-egg twins, with their diverse sets of genes, for comparison with the one-egg twins, having identical sets of genes, completes what is required for discovering just what resemblances and differences in human beings are due to identity and diversity of genes. The conditions to which the two members of a pair of twins are subjected are as much alike in the two-egg twins as in the one-egg twins. Therefore we can be certain that any differences between the two types of twins are due to differences in the genes, not to diversities of environment.

Comparison of one-egg twins (having the same genes), with two-egg twins (having different genes): Identical twins are extraordinarily alike in all physical respects. They are always of the same sex. Their faces and figures are so much alike that it is difficult to distinguish one from the other. They are alike in eye colour, hair colour, skin colour. Their facial features are of the same form and relative size. Their teeth are alike, even to the irregularities. Their stature and weight are very similar. Their finger prints are as much alike as those of the two hands of the same individual.

In all these respects the two-egg twins are often very different. They are no more alike than any other two members of the same family.

Identical twins are also alike in weaknesses, in tendencies to certain diseases. If one has tuberculosis or other constitutional disease at a certain time of life, the other one usually

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has it also at about the same time, even though the twins live apart. But two-egg twins do not show these resemblances.

All this demonstrates that all these physical characteristics in man depend on genes. They are alike in two individuals whose genes are alike, diverse in two individuals whose genes are diverse.

One-egg twins at times show certain physical differences, resulting either from certain features of the process of splitting the original egg from which the two were produced, or from the fact that one of the twins has been injured by accident or disease. From the former cause arise the facts that (1) sometimes one of the twins is right-handed, the other left-handed, and (2) one is sometimes more vigorous than the other. If the splitting of the original single egg occurs very early, before the right and left sides have become diverse, the two twins are alike in 'handedness' and in vigour; if the splitting occurs later they may be diverse in these respects. The effects of diversity of environment on twins we take up in a later chapter.

Mental Characteristics in Twins.—In a number of cases the two twins from a single egg have been separated while very young—before the age of one or two years, and have lived apart afterward. In such cases the genes of the two individuals are alike, while their environments have been different. What is the situation as to their mental characteristics?

Several cases of this sort have been very carefully studied by Muller and by Newman. We shall have occasion to look at the results of this study in some detail later (see Chapter 10). Here we may summarize briefly from our present point of view what was discovered. One-egg twins that have lived apart show the same close resemblance in physical characterization that is found in such twins as have lived together. They show also resemblance in mental characteristics: in emotions, temperament, and in 'intelligence' as measured by psychological tests. In certain cases, there are found some dissimilarities in mental and emotional characteristics, depending on differences in education and experience in the separated twins—a matter to which we return in a later

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chapter. Thus it is clear that (1) the genes have great influence on mental characteristics, emotions, temperament, and the like, but that (2) these things may be modified by different education and experience.

An illuminating study of the mental and moral characteristics of twins was made by Johannes Lange. He found in the prisons of Germany, or in the prison records, thirty persons, each of whom was a member of a pair of twins, the two members in each case being of the same sex. He traced and examined the other twin of each pair. Thus one twin was chosen because he was a criminal; the other twin was taken as he chanced to be. As it turned out, thirteen of the pairs were single-egg twins, while the other seventeen were two-egg twins.

Of the thirteen pairs of one-egg twins, one of which was known in each case to be a criminal, it turned out, upon investigation, that the other also had a criminal record in 10 out of the 13 cases. It is clear that if one such twin comes in conflict with the law, the other one, identical in original nature, has small chance of escaping that fate. But with the two-egg twins, made up of diverse original materials, the situation was different. Their environments were as similar as were those of the one-egg twins. But of the 17 pairs of this kind, in only three cases was the other member of the pair found to have a criminal record. In the other 14 pairs the fate of the two was quite diverse. One was a criminal in each case; the other was not.

Thus it is clear that everything that helps to determine whether a man shall be a criminal or a good citizen is deeply affected by the materials of which the individual is made, by his 'heredity'. Mentality, morality, conduct, career, fate, are affected by the hereditary materials with which the individual starts life.

The truth of this conclusion came out still more strongly when the detailed records of the twins were studied. In the case of the single-egg twins, the two members conducted themselves as duplicate personalities might be expected to do. One such twin was a burglar; on looking up his brother's

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record, he was found to be a burglar too. In another pair, one twin was a high-powered financial swindler, fraudulently collecting large sums from his dupes. And so also was the other twin of that pair. Besides the pair that were burglars, and the pair that were swindlers, another pair of one-egg twins both 'committed puerile offences against the property laws'. Another consisted, in the words of Lange, of 'gutter-snipes, but good fellows at heart', though they 'cannot stand alcohol; it develops frenzy and draws the knives from their pockets'. Another pair described 'have too little sense and will power', while in still another, both 'are lacking in all human feeling except for their own unpleasant selves'. And so goes the account throughout the entire list; the similarity in conduct is astonishing. Lange says, 'In all these pairs the type of crime is identical, the criminal careers begin at about the same age, and the behaviour of both members in court and in prison corresponds absolutely.'

But in the two-egg twins, that started life with different parental materials, with different heredity, the situation was different. As we have seen, 14 out of the 17 had totally different careers, one being a criminal, the other not. And there was no such detailed parallelism in the records of the two as was found in the one-egg twins. As before remarked, the similarity of environment was as great in the two-egg twins as it was in those that came from one egg. But this similarity of environment did not result in identity of fate or in detailed parallelism in careers. It was the identity of original nature, of the materials out of which they are made, that gave the same careers and the same fate to the one-egg twins. They were almost as much alike in their behaviour, their mentality, their career and their fate, as they were in their physical features—in which, like other one-egg twins, they were almost indistinguishable.

It is certain, therefore, that all the things that affect character and conduct are deeply influenced by the hereditary materials. There is no characteristic or quality of human beings that is exempted from its influence. This conclusion is confirmed by all the many studies that have been made on

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the two types of twins. And it is in harmony too with all that we know of the science of genetics. Experimental work on the breeding of other organisms shows, as we have seen, that they have no characteristics of any kind that are not affected by the genes that they receive at the beginning of their lives.

Are characteristics influenced also by other conditions, by the environment? The fact that all are affected by genes does not at all imply that they may not be affected in other ways. The influence of the environment is dealt with in Chapter 10.

NOTES AND REFERENCES ON CHAPTER 8

1. Page 180. For the evidence on duplicate genes in the shepherd's purse, see G. H. Shull (1914), 'Duplicate Genes for Capsule Form in *Bursa bursa-pastoris*', *Zeitschr. für Induktive Abstammungs- und Vererbungslehre*, Bd. 12, pp. 97-149.

2. Page 180. See W. E. Castle (1914), *Piebald Rats and Selection: An Experimental Test of the Effectiveness of Selection and of the Theory of Gametic Purity in Mendelian Crosses*, Carn. Inst. Publ. No. 195, 56 pages.

3. Page 188. M. Demerec (1934), 'Biological Action of Small Deficiencies of X-Chromosome of *Drosophila melanogaster*', *Proc. Nat. Acad. Sci.*, vol. 20, pp. 354-359.

4. Page 191. For inheritance of characteristics in man, see the references given at the end of Chapter 4.

5. Page 192. On the production of identical twins in the armadillo, see H. H. Newman (1913), 'The Natural History of the Nine-banded Armadillo of Texas', *Amer. Naturalist*, vol. 47, pp. 513-539.

6. Page 192. Many investigations and publications on twins, particularly in man, have been made of late; the subject is a most active one. The following may be consulted:

By H. H. Newman (1917), *The Biology of Twins*, 186 pages; (1923), *The Physiology of Twinning*, 230 pages; *Mental and Physical Traits of Identical Twins Reared Apart*; a series of articles in the *Journal of Heredity*, 1929 to 1934. By H. J. Muller (1925), 'Mental Traits and Heredity', *Journal of Heredity*, vol. 16, pp. 433-448. By N. D. M. Hirsch (1930), *Twins, Heredity and Environment*, 159 pages. By J. Lange (1930), *Crime and Destiny*, 250 pages.

9

RULES AND RATIOS OF INHERITANCE

In earlier chapters we have seen that the dependence of characteristics on genes located in the different chromosomes results in three diverse types of inheritance. Characteristics follow in descent from earlier to later generations the distribution of the particular chromosomes in which are the genes on which the characters depend. Since there are three different types of distribution of the chromosomes, there result three types of inheritance. These are: (1) sex-linked inheritance, dependent on genes in the X-chromosome; (2) autosomal (or typical Mendelian) inheritance, depending on genes in autosomes; (3) Y-chromosome inheritance, depending on genes in Y.

This dependence of characters on genes in the different chromosomes results, in later generations, in the production of certain numerical ratios among the individuals manifesting different characters. Of these the most common is the 3 to 1 ratio occurring in generation F₂, in autosomal inheritance.

In the present chapter we proceed to a systematic examination of the diverse inheritance types and ratios, in their relation to the characteristics manifested.

The most general principle underlying this matter, we shall find, is the following:

The type and ratio of inheritance of any character is a relative matter: it depends upon the relative genetic constitutions of the two parents and on the characters manifested by them. More specifically, the type and ratio shown in inherit-

ance by any character depends on what other character or characters it is mated with.

Many examples of these relations are found in the following pages.

In the early study of genetics it was commonly believed that each separably heritable characteristic, such as red eye or vermilion eye or rudimentary wings in the fruit-fly, depends on one gene only, and follows in its descent the distribution of that gene. Any characteristic that gave in heredity the simple Mendelian ratio (3 dominants to 1 recessive in F_2), or the simple sex-linked ratio, was considered a 'unit character', and was said to show 'unit character inheritance', depending supposedly on but a single 'factor' or gene. (The word factor came into use before the nature and location of the genes were known; it is still much used as a synonym for gene.) This single factor was supposed in some way to represent in the germinal material the character to which it gave rise. It was thus called 'the factor' or 'the gene' for that character, a form of expression which still persists, though its implications are erroneous.

Later it was discovered that this conception is a mistake, since every characteristic is produced by the interaction of many genes, and can be altered by changing any one of them. The reason why certain characteristics give in heredity the simple Mendelian or sex-linked ratio is that the two parents *differ* in but one pair of the many gene pairs that influence the character. If the two parents differ in more than one of the gene pairs that influence the character, more complex ratios result. Furthermore, the type of inheritance shown by a given character (whether sex-linked, autosomal, or of the Y type) depends on the location of the gene pair or pairs in which the two parents differ. These important relations, with the general principles underlying them, are illustrated in the following sections, which take up in order the types of inheritance, and the ratios that result when the parents differ in one or more gene pairs, whether in X, the autosomes, or in Y.

1. Parents differing in a single pair of autosomal genes.—

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As seen in the preceding chapter, the red colour of the eye in the fruit-fly depends on at least 19 gene pairs scattered in various parts of the four pairs of chromosomes (Fig. 41). An individual with the usual red eyes has all these genes in the normal or unmodified condition. Suppose that such an individual is mated with another that has all but one of these 19 gene pairs in the normal condition. This individual has the two genes of the pair at II, 54.5 (Fig. 41) so modified as to cause the eyes to be purple in colour. We may call these two modified genes *aa*, while the corresponding two unmodified genes may be designated *AA*. The chromosomes of the two parents will then be represented as in Fig. 44, P; they differ only in the genes at II, 54.5.

When germ cells are formed in the usual way by such individuals (one chromosome of each pair passing to each germ cell), and the germ cells from the two parents are mated, we of course find that all the individuals (zygotes) of F₁ have both the dominant normal gene *A* and the recessive gene *a*, so that they have the normal red eyes (Fig. 44, F₁).

When two of these individuals *Aa* of F₁ form germ cells, and are mated in the usual way, they yield in F₂ individuals of three different genetic constitutions, in the proportions $AA + 2Aa + aa$, or 3 dominant red to 1 recessive purple. The red and purple are inherited in the typical Mendelian or autosomal ratios for a single-gene difference, or as 'unit characters'.

(It is obvious that to obtain the correct constitutions and ratios in later generations no account need be taken of the parts of the genetic system that are alike in the two parents. All that is required is to represent by different letters the genes that differ in the two parents. The two parents may thus be called *AA* and *aa*, the F₁ generation *Aa*, the F₂ generation $AA + 2Aa + aa$. It is only when the conditions are complex that it is necessary to represent the chromosomes, as in Fig. 44.)

2. Parents differing in a single pair of genes located in the X-chromosome.—The same character red eye-colour, just considered, gives in other cases a different type of single-gene

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inheritance. This occurs when the recessive parent differs from the dominant red-eyed parent in a single gene or gene pair that lies in the X-chromosome.

Let the red-eyed individual be a male, the recessive parent a female having eosin eyes. The female thus differs from the male in having the recessive eosin gene in her X-chromo-

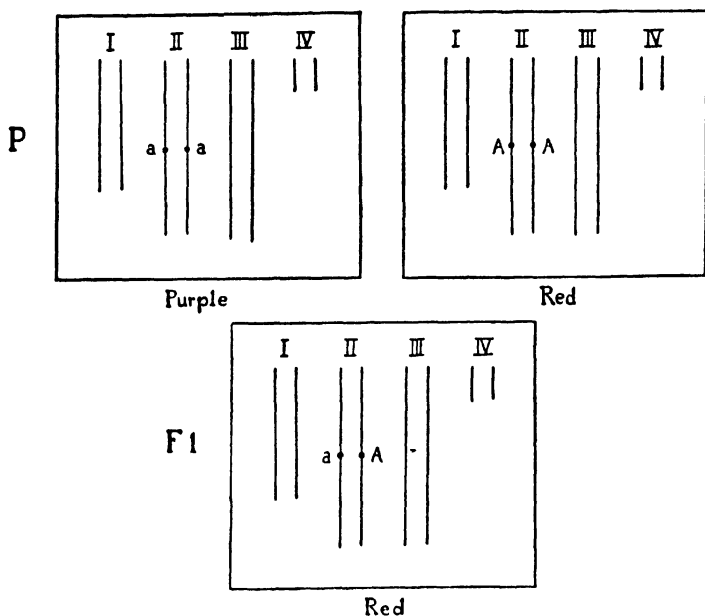


FIG. 44.—*Diagrams to illustrate the situation as to chromosomes and genes in a cross between parents differing in a single pair of autosomal genes, AA and aa. The usual algebraic expressions for such crosses, $AA \times aa = Aa$, are essentially abbreviated diagrams of this type, with the omission of all parts of the chromosomes in which the two parents are alike.*

somes, at the locus I, 1.5 (Fig. 41). Again represent the two recessive genes by aa . The corresponding normal gene in X will be called A , and as the male has but one X and therefore one gene A , it may be represented as AO (in which O represents the absence of this gene). We now have the situation:

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	<i>Males</i>	<i>Females</i>
Parents	AO Red eyes	{ aa Eosin eyes
Germ Cells	A and O	a and a
F ₁	aO Eosin eyes	{ Aa Red eyes

Thus the two eye colours now give sex-linked inheritance, with 'criss-cross' inheritance in F₁: the sons have eosin eyes, the daughters red eyes. If we mate together the males and females of F₁, forming the germ cells as usual, we obtain for the constitution of F₂ in this case:

Sons AO + aO; Daughters Aa + aa

That is, in F₂, half the sons and half the daughters have red eyes; the other half, eosin eyes.

Thus the same character, red eye-colour, which in the former case gave 'unit character' or 'single factor' inheritance of the autosomal type, gives in this second case 'unit character' or 'single factor' inheritance of the sex-linked type, with very different ratios. The way that the character red is inherited depends on what it is mated with.

Similar analyses can be given for all cases in which the two parents differ in but one pair, out of the many gene pairs on which depends the character examined. Thus in probably all cases in which characters give 'unit character', or 'single factor' inheritance ratios, the character is in fact affected by many diverse gene pairs, but only one pair differs in the two individuals that mate. The expressions 'unit character' and 'unit character inheritance' are still much used, but they should always be interpreted as meaning 'unit difference'; that is, as inheritance resulting from difference in a single pair of genes.

But if the parents differ in more than one pair of the genes on which the given character depends, the simple Mendelian or sex-linked 'unit character' ratios will not be produced, but more complex ratios. This may be illustrated for the same character, red eye-colour, as follows:

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3. Parents differing in two pairs of autosomal genes, in different chromosomes.—The red-eyed parent is mated with an individual that has two of the 19 eye-colour genes modified; one pair in chromosome II at 54.5 giving recessive purple eyes; another pair in chromosome III at 48.0 giving recessive pink eyes (see the maps, Fig. 38).

As before, we need to take account only of the genes in which the two parents differ. Call the two recessive genes that give purple eyes *aa*, the two that yield pink eyes, *bb*. Then the corresponding dominant genes in the other parent may be called *AA* and *BB*, these giving red eyes. It is necessary to keep in mind the eye colour in the different types of individuals. Those having only the two recessive genes *aa* have purple eyes; those with only *bb* have pink eyes; those with both *aa* and *bb* have purple-pink eyes. Those with neither pair of recessive genes have red eyes; these are *AABB*.

When the red-eyed parent *AABB* is mated with the purple-pink-eyed parent *aabb*, the results are those given in the analysis of page 113, Chapter 5, for parents differing in two autosomes. The *F*₁ generation all have the constitution *AaBb*, and since *A* and *B* are dominant, all the individuals of *F*₁ have red eyes.

Now mate together individuals of *F*₁; they yield the combinations shown in table 2, page 120. And as there shown, if we classify these as to the characteristics that are manifested (that is, as to what dominant genes they contain), the proportions are the following:

$$9AB + 3Ab + 3aB + 1ab$$

All those that contain both the dominant genes *A* and *B* have red eyes. Those that contain the dominant *A* but not the dominant *B* have pink eyes. Those that contain the dominant *B* but not the dominant *A* have purple eyes. Thus the individuals with different eye colours occur in *F*₂ in the proportions: nine red-eyed (*AB*) to three pink-eyed (*Ab*) to three purple-eyed (*aB*) to one pink-purple-eyed (*ab*). Or we can classify them as 9 red-eyed to 7 not red.

Thus in this case the character red gives in *F*₂ still different

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proportions from those that were found in the two previous cases. It now gives 'two-factor' autosomal inheritance. It illustrates anew the fact that the type and ratios of inheritance given by any character depend upon what it is mated with.

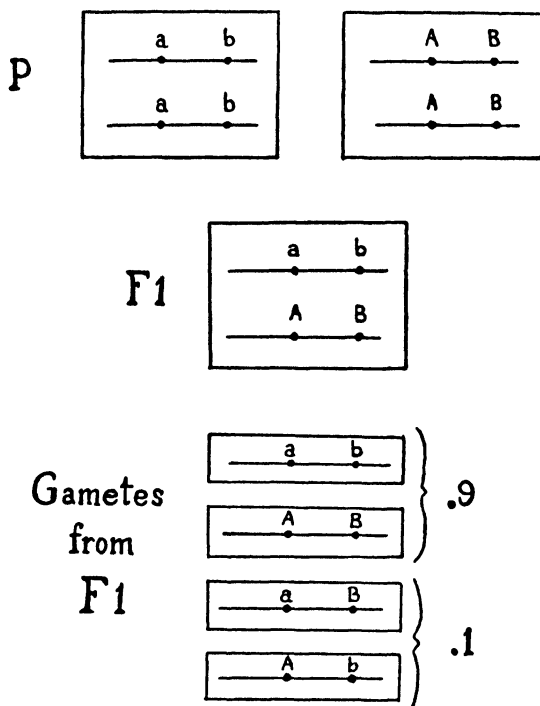


FIG. 45.—Diagram to illustrate the ratios produced in F_2 when parents differ in two gene pairs located in the same autosome. See text.

4. Parents differing in two gene pairs in the same autosome.—When the gene pairs in which the parents differ are located in the same chromosome, the ratios are altered by the fact that genes in the same chromosome usually go together to the descendants; that is, they show linkage. An ideal case will illustrate the results.

Let one parent carry the two recessive gene pairs aa and bb ,

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located in the same autosome. The corresponding dominant genes, in the other parent, may be called as usual AA and BB. The two parents will then show the constitution illustrated in Fig. 45, P. Their F₁ offspring will then be a heterozygote of the type shown in Fig. 45, F₁. Its two chromosomes may be designated A—B and *a—b*.

Assume that the distance between the two gene pairs is such that exchange takes place in one-tenth of all cases, the exchanges yielding chromosomes carrying A—*b* and *a*—B, in place of the original A—B and *a—b*. Then in nine-tenths of all cases the chromosomes retain the original constitution, A—B and *a—b*; in one-tenth they have the changed constitution A—*b* and *a*—B.

Now, when these chromosomes separate into different gametes, there will be formed four types of gametes having respectively the chromosomes A—B, *a—b*, A—*b*, and *a*—B (Fig. 45), and these four types will occur in the proportions just given. That is, of the entire number of gametes, the four types occur in the following proportions:

$$\cdot45AB + \cdot05Ab + \cdot05aB + \cdot45ab$$

Since it is only the relative proportions that are important, all terms of this expression may be multiplied by 20 to make them integral. They then yield the proportions

$$9AB + 1Ab + 1aB + 9ab$$

These different types of gametes mate in the above proportions with the gametes from the other parent. In such an organism as *Drosophila*, in which exchange of genes occurs only in the female, it is only the ova that will exist in the above proportions. The male, in which no exchange occurs, will produce but two sorts of gametes in equal proportions, those containing the chromosome A—B, and those containing the chromosome *a—b*. The sperms therefore are in the proportions:

$$\cdot5AB + \cdot5ab$$

Or, what is the same,

$$1AB + 1ab$$

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The zygotes of F₂ will then be produced in proportions given by mating each of the two types of sperms AB and *ab* with each of the four types of ova in the proportions in which they occur. The results are given simply by multiplying together algebraically the two expressions:

$$(9AB + 1Ab + 1aB + 9ab) (AB + ab)$$

This yields for the constitution of the generation F₂ the following:

$$9ABAB + 1ABAb + 1ABaB + 18ABab + 1Abab \\ + 1aBab + 9abab$$

Since the capital letters represent dominant characters, the characters A, B, *a* and *b* will be manifested in F₂ in the following proportions:

$$29AB + 1Ab + 1aB + 9ab$$

In case crossing-over (or exchange) occurs equally in both sexes, the constitution of the F₂ generation will be given by the product of the two expressions:

$$(9AB + 1Ab + 1aB + 9ab) (9AB + 1Ab + 1aB + 9ab)$$

This yields for the constitution of the F₂ generation individuals of different genotypes in the following proportions:

$$81ABAB + 18ABAb + 18ABaB + 162ABab + 1AbAb + 2AbaB \\ + 18Abab + 1aBaB + 18aBab + 81abab$$

If we classify these as to whether they manifest the characters represented by A, B, *a* or *b*, we find the proportions to be as follows:

$$281AB + 19Ab + 19aB + 81ab$$

The method of computing the results may be generalized as follows:

Call the two pairs of dominant genes AA and BB, the two pairs of recessive genes *aa* and *bb*. Then the one parent has the two chromosomes A—B and A—B, the other parent *a—b* and *a—b* (see Fig. 45). The individuals of F₁ then all have the two chromosomes A—B and *a—b*.

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Let r = the exchange (or cross-over) ratio (the proportion of cases in which the chromosomes exchange genes, in the germ cells produced by F_1).

Then $1 - r$ = the proportion of cases in which there is no exchange.

Then in the individuals in which exchange occurs (one or both sexes) gametes are produced in the proportions:

$$(1 - r)AB + rAb + rAB + (1 - r)ab \quad (1)$$

If in one sex there is no exchange, the gametes from the individuals of that sex are of but two kinds, in the proportions:

$$AB + ab \quad (2)$$

(Since in these expressions (1) and (2) it is only the relative proportions that are important, either or both may be multiplied through by any convenient factor to make the numbers integral; the factor need not be the same for both.)

The proportions of the different types of individuals (zygotes) in F_2 are obtained by multiplying together the expressions for the proportions of the gametes in the two sexes. That is, the proportions in F_2 are, if crossing-over occurs in one sex only:

$$[(1 - r)AB + rAb + rAB + (1 - r)ab] [AB + ab] \quad (3)$$

While, if exchange occurs in both sexes, the proportions in F_2 are:

$$[(1 - r)AB + rAb + rAB + (1 - r)ab]^2$$

The value of r in case of different pairs of genes is determined by extensive observation of the results of experimental breeding. For different pairs of genes of *Drosophila*, many such values of r are given in the various publications of Morgan, Bridges and Sturtevant.

5. Parents differing in two gene pairs of the X-chromosome.—In this case, ratios diverse from those given by autosomal genes will be produced, owing to the different method of descent of X. The two genes will show sex-linked inheritance, with linkage. It will be found an interesting exercise to give some definite value to r , the exchange or cross-over ratio,

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then to work out formulae for computing the proportions of the different types of zygotes in F₂.

6. Parents differing in two pairs of genes, one pair in X, the other in an autosome.—In this case complex ratios result for the composition of F₂. These can be worked out by representing in diagram the two kinds of chromosomes in the two parents and putting them symbolically through the processes of gamete formation and fertilization.

7. Parents differing in several pairs of genes located in the same or different chromosomes (autosome or X).—In such a case the computation of inheritance ratios is very complex. It must be done by representing in diagrams the different chromosomes and the position of the genes within them, then putting them symbolically through gamete formation and fertilization, taking into consideration the known exchange ratios.

8. Genes in the Y-chromosome.—In most organisms, seemingly few genes, or none, occur in the Y-chromosome. As they do occur in rare cases, it will be well to indicate the resulting ratios for certain different cases.

(a) A dominant gene A in Y, corresponding to a recessive gene *a* in the X-chromosome. This case is realized in *Drosophila*, in cases in which the X-chromosomes contain the recessive gene *bobbed*, which shortens the body bristles, while the Y-chromosome contains the dominant normal or wild-type gene causing the bristles to be of normal length. The two parents are then:

	<i>Females</i>	<i>Males</i>
Parents—	aa	aA
	Bobbed bristles	Normal bristles

Here the *a*'s are in the X-chromosomes, the A in the Y-chromosome. Since Y goes only to males, the F₁ generation will be:

<i>Females</i>	<i>Males</i>
aa	aA
Bobbed bristles	Normal bristles

This situation will continue in later generations: all the males dominant, all the females recessive.

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(b) The dominant gene may occur in some of the X's, as well as in Y. Suppose that the X of the male has the dominant gene A, as does also the Y, while the X's of the female have the recessive gene a. Representing the X that contains the dominant gene by A, while the Y that contains it is represented by A, the following is the situation:

	<i>Females</i>	<i>Males</i>
Parents:	aa	AA
	Recessive	Dominant
F ₁	aA + aA	aA + aA
	Dominant	Dominant
F ₂	Aa + aa	AA + aA
	Dominant Recessive	Dominant

In such a case, therefore, all the males are dominant in every generation. But in F₂, half the females are recessive, and recessive females will appear also in later generations.

(c) If Y contains a recessive gene, while the X's contain the corresponding dominant, the effects of the recessive gene will never be manifested, since both sexes carry the dominant X. Thus Y might contain many recessive genes, none of which would ever be manifested.

(d) In certain fish, crossing-over of genes from X to Y or vice versa has been described as occurring in rare cases. This of course changes the method of inheritance. Details need not be entered into here, since such cases are very infrequent.

9. In some cases, as will be shown in later chapters, when the chromosomes are broken into pieces by radiation, a piece of an X-chromosome may become attached to an autosome, remaining thus attached in later generations. In such a case the genes of this piece of X, which normally give sex-linked inheritance, after the breakage give autosomal inheritance. Similarly, a piece of an autosome may become attached to X, its genes thereafter yielding sex-linked inheritance.

Certain important special conditions, some of them classifiable, as to certain features, under cases already considered, are worthy of special consideration. These are the following:

10. Both parents recessive for a single pair of genes.—When

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two such recessive parents are mated, the nature of the characters shown by the offspring differs in different cases, depending on whether the recessive genes of the two parents are or are not alleles; that is, on whether they are or are not at the same locus of the same chromosome (compare Figs. 46 and 47).

A. The recessive genes in the two parents are alleles, being located at the same loci of the same chromosome (Fig. 46, c).

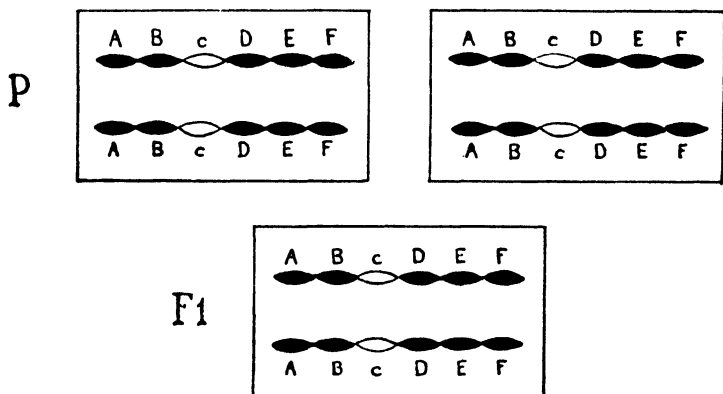


FIG. 46.—Diagram to illustrate inheritance of recessive characters in cases in which the two parents are recessive in genes that are alleles (belonging to the same pair). The offspring (*F*₁) manifest the recessive character.

In this case no corresponding dominant gene is present. All the offspring and descendants are therefore recessive. This is the result when the two parents are alike in their recessive characters, as when two eosin-eyed parents are mated. It is also the result when the characters of the two parents differ, though due to different alleles of the same gene; for example, when parents with eosin eyes are mated to parents with buff eyes—both of these characters being due to modification of the gene at I, 1.5 in *Drosophila*. In such a case the heterozygotes, containing the two different modifications of the gene, are either intermediate in character, or approach one of the recessive parents more closely than the other.

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B. The recessive genes in the two parents are not alleles, but are modifications of genes at different loci (Fig. 47). In such cases the offspring (F_1) show, not the recessive characters, but the normal or dominant characters. The reason for this is, as shown by Fig. 31, A, that each parent has the dominant allele for the recessive character of the other parent.

If the two pairs of recessive characters of one parent are bb and those of the other parent are ee , then the parent carrying

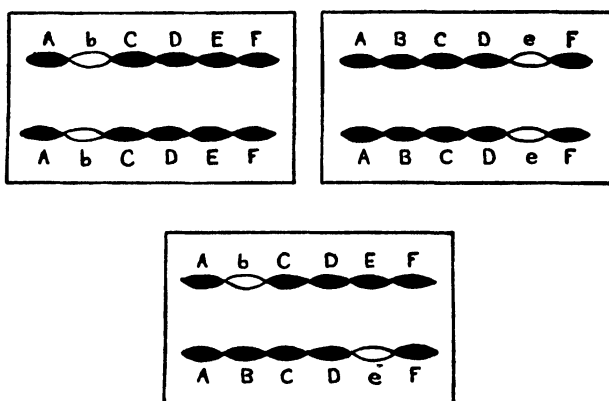


FIG. 47.—Diagram to illustrate inheritance in cases in which the parents are recessive for genes that are not alleles, but belong to different pairs. The offspring (F_1) do not manifest either recessive character.

bb has also the dominant genes EE , while the parent carrying ee has the dominant genes BB (Fig. 47). Thus the two parents are $bbEE$ and $BbEe$. Their offspring (F_1) are therefore $BbEe$; they have the dominant gene for both characters, and therefore manifest neither of the recessive characters (Fig. 47).

This is an extremely important relation. It holds both when the two recessive characters affect the same structure or function, and when they do not. Thus, if flies with eosin eyes are mated with those having vermilion eyes, the offspring all have normal red eyes. Or again, if vermilion eyes are mated with purple eyes, the offspring have normal red eyes. In such a case the recessive characters of the two parents may be indis-

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tinguishable; but, if they are not alleles, the offspring have the dominant character. Thus, as set forth on page 181, the eye colours garnet (gene at I, 44.4) and purple (at II, 54.5) are alike, but if garnet and purple parents are mated, the offspring have normal red eyes. Similarly, if rudimentary wings are mated with vestigial wings, the offspring have normal wings.

If the recessive characters of the two parents are quite diverse (and not alleles), the same rule holds: purple-eyed flies mated with vestigial wings yield offspring (F_1) that are normal both for eyes and wings.

11. Duplicate genes.—In certain cases a dominant character is produced in case a dominant gene of either of two pairs, AA or BB, is present, while the corresponding recessive character occurs only when both these dominant genes are lacking, so that in their place are two recessive pairs aa and bb. Such cases give special inheritance ratios; the proportion of dominants to recessives is 15 to 1 instead of 3 to 1. These are known as cases of duplicate genes.

We have before mentioned a case of this sort, described by G. H. Shull (1914) in the common weed *Bursa bursa-pastoris*, or shepherd's purse. Some races have dominant triangular pods, while others have recessive ovate pods. It appears that the race with ovate pods carries two recessive gene pairs, aa and bb, present in different autosomes. The race with triangular pods has two corresponding dominant pairs of genes, AA and BB, and the presence of a dominant gene of either of these pairs suffices to cause the production of the triangular pods. When these two races are crossed, therefore, the following is the situation:

Parents:	AABB	aabb
	Triangular	Ovate
F_1 :	AaBb	Triangular

When these F_1 individuals are bred together they of course produce in F_2 the sixteen sets of individuals of the constitutions shown in table 2, page 120. As examination of this table shows, 15 out of the 16 contain either A or B or both; hence

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these 15 have triangular pods. Only one of the 16, that with the constitution aabb, contains neither A nor B; this one has therefore ovate pods. Thus in such cases the ratio in F₂ is 15 dominant to 1 recessive.

A considerable number of such cases are known, yielding the ratio 15 to 1. They occur mainly in plants. In certain cases there are indications of a ratio of 63 dominants to 1 recessive in F₂. This is evidence that the dominant condition is produced if any one of three dominant genes, A, B or C, is present, while the recessive condition occurs only in individuals of the constitution aabbcc.

12. 'Blending inheritance.' Intermediate characters. 'Multiple factors.'

There are many cases in which a cross between two differing stocks results in progeny (F₁) that are intermediate between the two parent stocks, and this intermediate condition may continue, in large measure, in later generations. Such intermediate or blending inheritance is found mainly in characters that grade gradually from one extreme to another: dimensions, degrees of colour, and numerical characters, such as numbers of leaves in certain plants. A cross between large and small individuals commonly results in progeny that are intermediate. Crosses between whites and negroes give offspring that are intermediate in colour.

It was at first supposed that such 'blending' inheritance is of a fundamentally different type from Mendelian inheritance, that is, from inheritance depending on differences among the genes. This was an almost necessary conclusion when it was believed that each Mendelian character depends exclusively on a single factor or gene. But since it has been discovered that every character depends on many genes, and that parents may differ in one or many genes affecting a particular character, so-called blending inheritance has lost its unique character, and has been recognized as resulting, like other inheritance, from differences between the genes of the two parents. Many intermediate conditions have been discovered between ordinary single-gene inheritance and the phenomena of blending inheritance. These, with the evidence

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for the dependence of blending inheritance on gene differences, are set forth in the following.

A. Lack of dominance: heterozygotes intermediate.—In some cases, as we have seen on earlier pages, when two parents differing in a single gene pair are mated, neither character shows dominance. The offspring (F_1) from the mating are intermediate between the two parents, or show some blend of the two differing characteristics. That is, if the genes of the two parents are AA and aa , the heterozygotes Aa are not like either parent, but show a blend of their characteristics.

This is the usual case, as before seen (page 210), when parents showing two diverse recessive alleles are mated in *Drosophila*. Thus if eosin eye is mated with buff eye, the progeny (F_1) show eyes of intermediate colour; if vestigial wings are crossed with antlered, the progeny (F_1) show wings of intermediate type.

Many cases of this sort are known in various organisms. One of the best known is that of the Andalusian fowl. Here a black individual (AA) mated to a white one (aa) gives in F_1 individuals (Aa) that show a somewhat intermediate colour known as blue. Similar cases are known for plant and animal colours of various sorts. The heterozygote in such cases is frequently not closely intermediate between the parents; in different cases it shows various intergradations of the parental characters.

In such cases of lack of dominance, the ratios in which the different characters appear in later generations are changed; the familiar 3 to 1 ratio does not appear. If the parents are designated AA and aa , then the heterozygotes Aa of F_1 are all intermediate. When these are bred together, they yield the usual proportions:

$$AA + 2Aa + aa$$

Thus there are in F_2 three grades, one (AA) like one parent, one (Aa) intermediate, and the third (aa) like the other parent. And these three grades occur in the proportions 1 : 2 : 1. Here we have a simple example of what in more complex cases is known as blending inheritance.

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B. Dependence on differences in several or many gene pairs, having quantitative effects: 'Blending inheritance', 'Multiple factors'.

As before seen, any characteristic is affected by many different genes, though if the parents differ in but a single one of these gene pairs, the result is 'single-gene' or 'unit-character' inheritance. But the parents may differ in two or more of the genes affecting the characteristic, then yielding inheritance in various complex ratios. The gene pairs in which the parents differ may have qualitatively diverse effects, as in the case of eye colour in *Drosophila*, or coat colour in rodents.

But in other cases the different genes affecting the character differ only quantitatively in their effects. Thus, in peas, one of the cases studied by Mendel was a cross between tall and dwarf peas. These differed in a single gene pair; one of these (AA) gave tall plants; the other (aa) gave short plants. The gene A for tallness was dominant, so that the heterozygotes Aa were tall.

When such cases of quantitative difference in effects are combined with the production of intermediate conditions in the heterozygotes, and particularly when the parents differ in several gene pairs, or 'multiple factors', the result is to produce many gradations of the characteristic, so giving rise to what has been called blending inheritance.

Such inheritance, as before remarked, is seen particularly in such matters as dimensions, numerical characters, gradations of colour, and the like. But, as just seen, in some cases such characters depend on single-gene differences between the parents; they then give typical Mendelian or sex-linked ratios in the descendants.

Dimensions thus giving typical single-gene inheritance are: tallness and dwarfness in peas, in sweet peas, in *Antirrhinum* (the snapdragon), in tomato plants. Long and short styles in *Oenothera*; long and short wings in *Drosophila*; long and short hair in various rodents; long and short legs in Dexter-Kerry cattle; long and short fingers in man. Differences in colour that give typical Mendelian inheritance are numerous in *Drosophila*.

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In other cases of difference in dimensions or colour, or the like, the progeny are intermediate between the parents, and there may be many different gradations. This is the case for stature in man, for ear length in rabbits, for depth of colour in negro-white crosses, for many dimensions in organisms.

The key to the understanding of these cases was given by the discovery that, when such crosses occur, the descendants in the F_2 generation are much more varied than those in the F_1 generation. This is, of course, necessarily the case if the characters depend on differences in genes. When parents differ in a single pair of genes AA and aa , the offspring all have in F_1 the same constitution, Aa . But in F_2 there are three different constitutions $AA + 2Aa + aa$, so that F_2 is much more varied than F_1 . Again, suppose that the parents differ in two pairs of genes, so that one parent is $AABB$, while the other is $aabb$. Then the F_1 generation all have the constitution $AaBb$, and are therefore all alike. But in the F_2 generation there are nine diverse combinations of the genes, as shown in table 2, on page 120; they therefore show much more diversity than occurs in F_1 .

An illustration will show how this works. Suppose that two races differ in size, in consequence of a difference in two pairs of genes. The larger race carries the genes $ABAB$, while the smaller one has the corresponding genes $abab$. Assume that each one of the four genes $ABAB$ increases the size by a certain amount above that of the race $abab$. When the two races are crossed, the F_1 generation all have the constitution $ABab$. Having two of the four genes that increase the size, they are intermediate in size between the two original races, and, as all have the same constitution, there will be little variation in size.

Now mate together two of these individuals $AaBb$. These will give for the F_2 generation the combinations shown in table 2, page 120. Of these, those that have four of the genes $ABAB$ will be largest, those with but three of them will be smaller, and so on down to those having none of them—the individuals with constitution $abab$. There will thus be a series of graded sizes. To determine the relative number of

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individuals in the different grades, from smallest to largest, list from table 2 (page 120), the constitutions having respectively 0, 1, 2, 3, or 4 of the 'size genes' ABAB. The result is as follows:

Number of size genes	0	1	2	3	4
	<u>abab</u>	abaB	abAB	ABAb	<u>ABAB</u>
	1	aBab	aBAb	AbAB	1
		abAb	ABaB	ABaB	
		<u>Abab</u>	<u>ABab</u>	<u>aBAB</u>	
		4	AbAb	4	
			<u>aBaB</u>		
			6		

Thus there are in F₂ five grades as to size. The most numerous individuals (6 out of 16) have the intermediate size, with but two of the 'size genes'. There are 4 a little smaller and 4 a little larger, with a single individual in each of the extreme classes. The numbers of individuals in the different classes are given by the binomial series resulting from expanding the expression $(1 + 1)^4$.

Similarly, if the two original races differ in three pairs of genes in different chromosomes, so that one is AABBCC, while the other is aabbcc, the F₁ generation will have the uniform constitution AaBbCc, and so will be intermediate between two races. The F₂ generation will be found to have seven size gradations containing respectively 0, 1, 2, 3, 4, 5, or 6 of the 'size genes' AABBCC, the different grades showing the following relative numbers of individuals:

No. of size factors	0	1	2	3	4	5	6
No. of individuals	1	6	15	20	15	6	1 = 64

Here the relative numbers of individuals in each of the grades is given by the expansion of the binomial $(1 + 1)^6$. The relative numbers for any other number of 'size genes' can be written out directly. For four pairs the series is given by $(1 + 1)^8$, and for n pairs it is $(1 + 1)^{2n}$.

Thus when there is a cross between races differing quanti-

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tatively in size, depth of colour, or the like, the difference being due to a diversity in several pairs of genes, the general results are as follows:

(1) The F_1 generation is uniform (except in so far as there are variations due to environmental conditions), and is intermediate between the two parental types.

(2) The F_2 generation is varied in constitution. It consists of a series of grades, varying from the larger to the smaller parent. If the number of gene pairs in which the original parents differ is n , the number of grades is $2n + 1$.

(3) The number of individuals is largest in the intermediate grades, and decreases toward the more extreme grades, in both directions.

(4) The relative numbers of individuals in the different grades, from smallest to largest, are given by the expansion of the binomial $(1 + 1)^{2n}$.

(5) Since most of the individuals fall in the intermediate grades, the general effect is to give the impression that F_2 , like F_1 , is intermediate, so that the inheritance appears to be of the blending type. This is particularly true if only small numbers of individuals are available for study; most or all of these fall in the intermediate classes.

(6) But careful study, when large numbers of individuals are available, shows that the F_2 generation is much more variable than the F_1 generation. It reveals also the presence of a few extreme individuals, differing little or not at all from the two parental types.

This greater variability in F_2 as compared with F_1 , in cases in which the parents differ quantitatively, has been found to occur in great numbers of cases, of which the following may be mentioned: size and shape in gourds, squashes, beans (Emerson, 1910); length of the ears in maize (East and Hayes, 1911); colour, size of seeds and of petals in flax (Tammes, 1911); time of flowering in peas and in cotton (Tschermak, 1911); size in ducks (Phillips, 1912); winter hardiness in cereals (Nilsson-Ehle, 1912); skin colour in negro-white crosses (Davenport, 1913); size in rabbits (MacDowell, 1914); and in many other cases. There appears to be no known case

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of 'blending inheritance' in which the F₂ generation is not more variable than the F₁ generation, so that it appears clear that in all such cases the inheritance is based on differences in a number of genes ('multiple factors'), each of which has a quantitative effect on the characteristic.

(7) The later generations, produced from the interbreeding of the F₂ individuals and their descendants, show much the same relations as are found in F₂. Most of them are intermediate, though with a number of different grades. A few are extreme; these, however, are so rare that they are observed only when large numbers are bred.

(8) The intermediate individuals in F₂ or later generations, when interbred or self-fertilized, usually do not breed true; they produce a number of different grades, so that their offspring are variable. This is because the intermediate individuals (*a*) include a number of different grades, with different constitutions; also (*b*) many of them are heterozygotic. The commonest intermediates are those with the constitution AaBbCc, etc., others show such constitutions as AaBBCc, AabbCc, and so on. These when interbred must give individuals of many different constitutions.

(9) The rare extreme individuals—for example, those that are very large or very small—when bred separately commonly 'breed true', producing offspring like themselves. This is because such extreme individuals are (*a*) all of the same constitution, and (*b*) homozygotic. The extreme individuals at one end of the scale have the constitution AABBCc, etc.; when two such homozygotes are bred together, they can produce only homozygotes like themselves. The extreme individuals at the other end of the scale have the constitution aabbcc, etc.; these also are homozygotes and can therefore produce only offspring having the same constitution as themselves.

(10) Results of Selection.—The peculiar relations set forth in paragraphs (8) and (9) above come out strongly in experimental work on the results of selection, in relation to quantitative differences—sizes, weights, yield of crops, and the like. Attempts were early made to improve the breeds of cultivated

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plants and animals by selecting and breeding together those of the better grades. The results were found to be as follows:

(a) If parents above the average are selected, these give offspring above the average, but varying.

(b) If from these offspring those of higher grade are selected, again these give offspring of higher grade, but varying. Thus by repeated selection of the higher grade individuals in successive generations, progressive improvement is produced, 'selection is effective'. Such selection in the opposite direction is equally effective.

(c) But after this has continued for a number of generations, improvement ceases; no further progress is made. Selection ceases to be effective. The individuals of the highest grade, when bred by themselves, produce offspring like themselves, without genetic variation, and the same is true for the individuals of lowest grade.

This cessation of the effectiveness of selection after a certain grade was reached was unexpected, and gave origin to much discussion. But after it became clear that in such cases multiple factors are at work, in other words that the various grades depend on the number of certain types of genes that are present, the matter was cleared up. Selection is effective so long as it deals with the intermediate grades, which are of various different genetic constitutions, and are frequently heterozygotic. But as soon as the homozygotic individuals AABBCc, etc., or aabbcc, etc., are reached, no further progress can be made, since these can produce only offspring having the same constitution as themselves.

On the whole it is fully demonstrated that so-called blending inheritance is inheritance resulting from gene differences, such as yield ordinary Mendelian inheritance; but in blending inheritance the parents differ in several or many pairs of genes, each gene having a quantitative effect.

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RELATION OF CHARACTERISTICS TO ENVIRONMENT

Its Interaction with Heredity

We have seen in earlier chapters that all characteristics of organisms, of whatever kind, depend on genes and can be altered by altering genes. This is no more than to say that all properties of organisms, as of inorganic bodies, depend on the materials of which they are made, and can be altered by altering those materials. Changing the genes alters the materials of which organisms are made, and thus may alter any of their characteristics.

But this leaves open the possibility that other things also may alter any or all of the characteristics. The fact that alteration of genes changes characteristics does not preclude their alteration by the conditions to which the organism is subjected during its life and development. In the present chapter we examine the action of environmental conditions on characteristics and their interaction with the genetic constitution.

To form a correct conception of the interaction of environment and genetic constitution, one must look at the method of manufacture of an organism: that is, at the nature of the process of development from an egg to an adult. To certain features of this we now turn.

Relation of Gene Action to Internal Environment in Individual Development

The organism starts as a single cell, the fertilized egg cell. This contains the great number of genes, a thousand or so, grouped together in the visible chromosomes.

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These chromosomes are seen to go at once to work. They are embedded in a mass of material, the cytoplasm, forming the body of the cell. They take up material from the cytoplasm, so that they swell, enlarge, become vesicles, become crowded together to form what we call the nucleus (see Fig. 15, Chapter 2). They chemically change this cytoplasm; they give it off again into the cell, so that the chromosomes are again minute condensed bodies. The changed cytoplasm that they have given off into the cells alters the nature and structure of the cell, often in a strongly marked, visible way.

This process of changing the cytoplasm by the action of the genes is the fundamental thing in development. The genes repeat this process over and over again—taking in cytoplasm, modifying it, giving it off in changed condition—leaving the genes themselves unaltered.

While this is going on, the cell divides into 2, 4, 8 cells, and so on. The different cells receive diverse kinds of the cytoplasm that has been worked over by the genes. So the different cells gradually become diverse. As the cells divide, each chromosome divides, each gene divides, and half of every gene goes into each cell, where it grows again to the original size. Thus every cell of the body contains all the genes, the complete set. The cells differ in their cytoplasm; they do not differ, as a rule, in their genes.

The cells keep getting diverse, in this way, till some produce bones, some muscles, some nerves, some eyes, some hands, till finally we have the complex individual with all his parts and functions.

How does it happen that the different parts of the body become diverse? Since all the genes are present in all the cells, why do not all the cells change in the same way, instead of becoming different?

Not very much is known about this; it is one of the darkest questions of biology. But some things are known about it that are of great interest for the question as to the effects of environment. Look at one or two experiments.

The original single cell divides into two cells A and B.

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These two cells later produce the two halves of the body; that is, one produces the right half, the other the left half.

Why does the cell A produce only the left half of the body instead of the whole body? Try separating the two cells. This can be done, with some difficulty, in certain organisms. Now we find that this cell A, when separated, produces, not the left half of the body, but the entire body, an entire individual; and the right-hand cell B will do the same.

So it is clear that what each cell produces depends on its environment, on its relation to the other cells. Separate the two; then the genes in each produce an entire individual, in place of half an individual.

This sort of thing turns out to be typical for development. Every cell contains as a rule all the genes, and so far as genes are concerned could produce an entire individual. But after a while, through the continued activity of the genes, many different substances have been manufactured from the cytoplasm and are located in the different cells. Things have now changed so much, and have become so fixed, that the genes can no longer start anew from the beginning. At such a later stage therefore a single separated cell will no longer produce an entire organism, or any required part of the organism, although it still contains all the genes. With age the cells become fixed in their ways, as old individuals do.

But this condition in which any cell can produce any one of many different parts of the body, depending on circumstances, may continue into a rather late period of development, particularly in the vertebrates. At a certain time the egg of such a creature as the frog has become a mass of small cells. Under normal conditions, when we examine this mass, we can predict what part of the adult each part will produce. Cells here will produce the brain, there at the sides the eyes, here the ear, there the spinal cord, here parts of the skin. If we leave the egg to itself, these are indeed the parts that will be produced.

But this is not because each cell can produce only that part and nothing else. For it is possible to cut off a disk of cells from the egg and turn it around, so that what was in front is now behind, what was right is now left. And now we find that

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all the cells change their method of action. The cells that would have produced brain now produce skin; what would have yielded skin now yields brain or eyes; what would have given spinal cord now produces cerebral hemispheres. What happens is that from a certain spot on the egg—a recognizable spot—an organizing influence starts out, so that this spot is known as the organizer, or the organization centre. This organizing influence, whatever its nature, creeps from cell to cell, causing each cell to alter internally—through the interaction of its genes and cytoplasm—in such a way as to produce the structures of the embryo. Each cell that is reached later transforms in such a way as to fit the cells that have gone before—in such a way as to make the next proper part in the pattern of the body. At a certain point the cells transform into spinal cord, the next ones into medulla, those next into midbrain, the next into forebrain, those at the sides into eyes, farther forward into skin. This organizing influence passes through, in the same way, whichever cells are present, so that it is clear that any of the cells can produce any of the parts that are to be produced. If one turns them side by side or end to end, the results are the same. Any cell can produce almost any of the parts of the body.

That is, then, from the beginning the cells adjust themselves to their surroundings, to their environment. What part of the body each cell becomes is determined, not by the genes it contains—for each contains all the genes—but by the conditions surrounding it. The genes within the cell are enormously sensitive to their environment, to the cells surrounding them. They alter their method of action to fit the situation, producing whatever is the next thing in the body pattern. Development is fundamentally adjustment to environment—in this case, to cellular environment.

Of course, what the genes may produce is not without limits. The genes of a frog produce the parts of a frog's body; the genes of a man produce the parts of a man's body. The genes of a Chinese produce the body of a Chinese; the genes of a Caucasian, the body of a Caucasian. Some genes produce an individual of light complexion; others, individuals of dark

complexion. Just what the gene shall produce in development is always dependent both on the nature of the genes that are at work and on the conditions in which they find themselves. And in this they give a true picture of the interactions of heredity and environment.

The dependence on the conditions surrounding the cells, of what the genes within the cells produce, is shown in certain other ways, in the production of differences of sex, of which some account is given in Chapter 3. As there seen, in many organisms the two sexes begin life with different chromosome combinations: one sex has two X-chromosomes, the other but one. It is to this original difference in gene combination that the later sex difference is ultimately to be referred. But the original difference in chromosomes acts through intermediate chemical products, and it is these diverse chemical products that cause the bodies of the two sexes to develop differently. In the embryo containing but one X-chromosome a certain kind of hormone is produced, in that having two X-chromosomes another sort of hormone. These two diverse hormones then circulate through the two bodies; they act diversely in the two, causing one to produce the characteristics of the male sex, the other the characteristics of the female sex. Body cells of either type (as set forth in Chapter 3) may produce either type of characteristics, depending on the hormone that acts upon them. That is, what their genes produce depends on the chemical conditions that surround them. Diversity of sex, like diversity in tissue differentiation, is produced through adjustment of the cells to their environment; in this case to hormonal environment.

It has been discovered that many other diversities between individuals, and between parts of the body, are produced by other kinds of hormones, by hormones secreted by the thyroid gland, by those from the hypophysis, and from other parts. Details cannot be entered upon here, but what they agree in showing is this: The genes first act to produce different chemicals. Then these diverse chemicals cause the cells to develop in certain particular ways, so as to give rise to diverse parts. By this continued interaction of genes with cytoplasm,

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of cells with each other, of cells with their surroundings, there is finally produced the entire body with all its parts and functions.

Thus in the process of development, adjustment of the cells to their environment, response to the surrounding conditions, play a fundamental part. The genes show themselves most sensitive to the conditions surrounding them.

Since genes act by producing hormones, and these hormones then determine many features of the later development, the question arises as to whether such hormones might not be provided in some other way. Could they be introduced into the body with the food, or by injection into the blood? If so, the characteristics produced would be controlled from outside. Or can the hormones be modified, or removed, in such a way as to change the characteristics of the individual?

As before seen (Chapter 3) this can indeed be done. The hormone produced by the male embryos (those having the single X-chromosome) may be transferred to the embryo that would otherwise produce a female, and cause it to produce male characteristics. In a similar way, the action of an imperfect thyroid hormone can be supplemented from outside. Individuals in which the genes supply a poor thyroid hormone fail to develop normally; in man they form the cretin, whose mental development is stunted. But this lack may be supplied by introducing the thyroid hormone with the nutrition; thereupon the development returns to its normal course.

In these cases products of the genes are transferred from one individual to another, where the same effect is produced as would result if the substance came from the operation of the individual's own genes. But a further step is possible. In some cases the chemicals controlling development are produced artificially and introduced into the developing body, where they produce the same effect as those produced by the organism itself. The active principle of the thyroid has been synthesized, and this synthetic product may be used in place of that produced by the genes, with the same effect on the development of the individual. Progress has been made in producing artificially other products of the genes, such as

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epinephrin, the secretion of the suprarenal body, and insulin, the internal secretion of certain cells of the pancreas. The production and use of hormones or endocrine secretions, and the control of development or function through their use, has become a vast chapter of physiology, which is enlarging rapidly. It all illustrates the fact that control of development and of characteristics is in large measure possible, and even at the present time is in a considerable degree practicable.

Altogether, therefore, it is clear that the processes of development and the determination of the nature of characteristics are not shut off from outside influence; but that, on the contrary, adjustment to the conditions is one of the fundamental features of development.

Thus far we considered mainly the rôle of environmental conditions in determining the different characteristics of different parts of the body. Do environmental conditions likewise play a rôle in determining the different characteristics of different individuals, so that individuals that have developed under different conditions have different characteristics? From what has just been set forth on the nature of development, this might be expected. We have seen that some of the characteristics developed depend on the hormones that are produced within the body. It is known that the production of some hormones is under the influence of the nervous system, and, through this, under the influence of outer conditions. This is the case in man with the hormone from the suprarenal capsules. This hormone affects behaviour, but little is known as to its effect on development. Other hormones, however, are known to affect development profoundly. Hormones from the hypophysis have a striking effect on growth. Differences in the quality and quantity of these hormones in different individuals result in the production of giants in some cases, of dwarfs in others, of normal growth in still others.

In another vertebrate a striking effect on development, altering all the adult characteristics, is known to be produced through the action of a hormone. The axolotl (Fig. 48, A) is a large salamander that has large red external gills, a tail

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flattened sidewise, for swimming, and other features that fit it for living in the water. It lives in the water thus all its life, becomes mature, produces eggs and young; there it dies; it is never anything but an axolotl.

But if it is fed on thyroid, it undergoes a transformation comparable to that which changes a tadpole into a frog. It

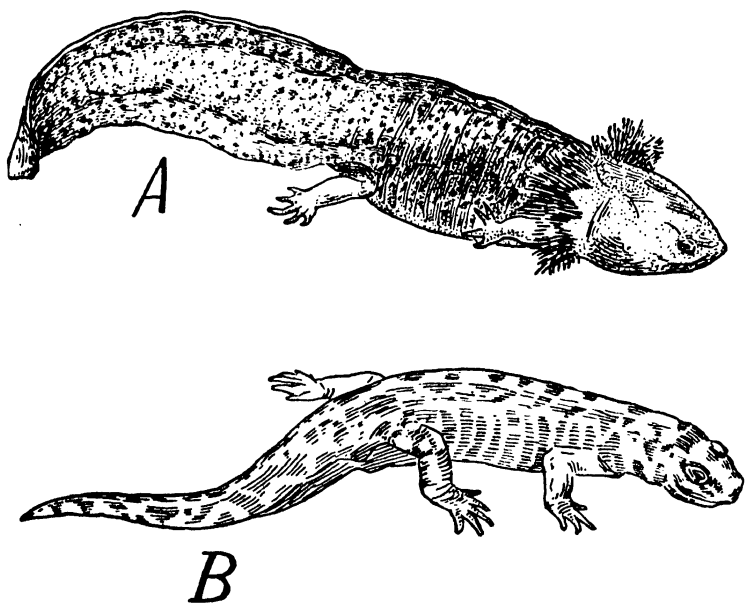


FIG. 48.—*Axolotl* (A), and *Amblystoma* (B), to show the difference in form and structure. Figures modified from those in Brehm's *Thierleben* (1912).

loses its gills; its body form becomes greatly changed, its tail is no longer flattened sidewise. It becomes fitted for living on land, crawls out on the land, and is the creature known as *Amblystoma* (Fig. 48, B). It now lives all the rest of its life under this guise, as a land animal; it becomes mature in this condition, producing eggs and young.

Of greatest interest from our present point of view is the fact that external conditions may induce this same transformation. If the axolotl is driven to come out on land under

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certain conditions of temperature and the like, it transforms into an *Amblystoma*, just as it does when fed on thyroid. There is little doubt that what these conditions do is to cause the thyroid of the animal to discharge its secretion into the blood, and that this induces the transformation. Thus the axolotl may have either one or two very diverse sets of characteristics, depending on the conditions that it meets during development.

Characteristics affected both by Genes and by Environment

Any of the characteristics of the organism may be altered by changing its genes: this we have seen in earlier chapters. Many of the same features that can be altered by changing the genes can likewise be altered by appropriate changes in the environment. Characteristics do not fall into two classes, one exclusively hereditary (or dependent on genes), the other exclusively environmental; but any characteristic is affected both by the materials of which the organism is composed, and by the action of the conditions on these materials.

Yet, as we shall see, in practice some characteristics are more readily altered by environmental conditions than are others. Certain characteristics owe most of their peculiarities to diversities among genes. Others are readily affected both by genes and by environment. Still others depend mainly on environmental conditions.

Particularly illuminating are the cases in which characteristics depend in marked degree both on genes and on environmental conditions, so that they are altered by changes in either. A number of well-known cases of this kind will be presented, selecting those that are from a technical point of view fully known.

In that animal whose genetics is best known, the fruit-fly *Drosophila*, many of the characteristics that have been studied are defects or abnormalities which are sharply dependent on the presence of particular genes. Such a one is abnormal abdomen (Fig. 49). This appears in the fact that

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the abdomen is ill formed, the segments not being regular nor sharply marked off. This abnormality is found to be due to a defect in a certain gene of the X-chromosome, so that it shows sex-linked inheritance, the abnormality being domi-

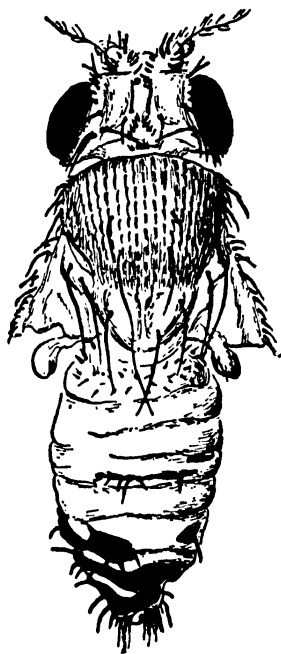


FIG. 49.—*Abnormal abdomen in Drosophila*, a characteristic resulting from a defective gene in the X-chromosome, but manifested only when the organisms are grown in a moist atmosphere. (Wings removed, to show the irregularity of the abdominal segments.) After Morgan and Bridges (1916).

nant.¹ Unless that particular defective gene is present the abdomen is normal. But it is dependent too on the environment. Individuals with the abnormal gene, if developed in a moist atmosphere, have the abnormality. But if those same individuals are developed in a dry atmosphere, they have normal abdomens. To produce the abnormal abdomen, we must have first the particular kind of defective gene that

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yields it. But second, even if that is present, we must have, too, the moist atmosphere for development; without it the abnormality is not produced, whatever the gene.

Another character in the fruit-fly that acts in a similar way is what is called reduplicated legs (Fig. 50). If a certain defective gene is present in the X-chromosome, the animals

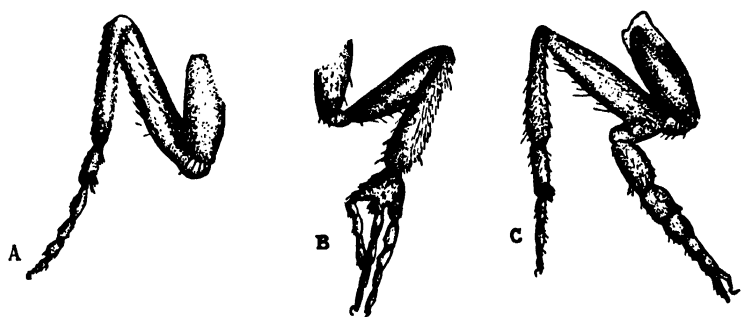


FIG. 50.—*Reduplicated legs in Drosophila, a characteristic resulting from a defective gene, taken in connection with development at a low temperature. A, normal first leg. B and C, legs showing different types of reduplication. After Hoge (1915).*

show a tendency to produce double legs, or even triple or multiple legs, in place of single ones.² But this does not happen unless the young develop at a low temperature. To produce reduplicated legs, then, there must be present a certain type of gene, and also a certain external condition. Unless both are present, the peculiarity is not produced.

It is clear from these cases that even though an individual inherits the type of gene necessary to produce a certain defect, it may not be inevitable that he should have that defect. A special environment may correct what inheritance leaves imperfect. These considerations apply to many things in man as well as in other organisms.

Another example of the fact that what is produced in development depends both on the genes and on the environment is seen in the production of giants in the fruit-fly.³ A modified gene, located in the X-chromosome, near its left end,

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causes the animals (if they have no other type of X-chromosomes than this) to become giants; they grow to nearly twice the size of the ordinary fly. But this increase in size takes place only if the animals having the modified gene are well fed during a certain period of their early lives. If not well fed at this particular time in life, they grow no larger than the usual flies. The giant size requires to produce it a particular type of environment acting on a particular type of gene. If either condition is not fulfilled, giants are not produced.

Again, in plants, the difference between green plants, containing chlorophyll, and white ones, is in some cases due to a difference in genes. Plants with a certain kind of genes will remain white even though grown in the light. In other cases, the difference between white and green plants is not the result of a difference in genes, but of a difference in environment. Plants that live in the dark remain white, even though they contain genes that can produce chlorophyll, while similar plants grown in the light are green. That is, to produce chlorophyll, a certain type of genes is necessary, and also a certain type of environment.

Again, there are red and white varieties of primroses; the difference in colour is inherited; it is due to gene diversities. But a certain variety produces red flowers when grown in a cool place, white flowers when grown in a warm, moist region, as in a greenhouse. The same diversity in colour is now due to an environmental difference.

Complex interrelations of genetic and environmental action have been described by Emerson with relation to diverse colours in maize plants.⁴ In different types, the leaves, the husks, the flowers, and other parts, differ in colour. Emerson describes and figures six main types, under each of which are subtypes. These are the following:

1. Purple, with its subtype, weak purple.
2. Sun-red, with a subtype, weak sun-red.
3. Dilute purple.
4. Dilute sun-red.
5. Brown.
6. Green, with a number of subtypes.

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The interrelations of genetic and environmental factors in these colours may be summarized as follows:

A. Each colour and each subtype is constant and hereditary, when the different types are bred under like conditions.

B. Each of the colours depends on many different genes, like the eye colour in *Drosophila*; they may be altered by changes in any of these genes. The different colours result from different combinations of the genes.

C. When the different types are crossed they give typical Mendelian inheritance: in some cases with simple ratios, in others with complex ratios.

Thus far the conditions are those for typical hereditary characters; the differences are the result of gene differences, and they follow the distribution of the different types of genes in inheritance.

But, also, the colours depend on the conditions to which the plants are subjected while developing. Change of certain conditions changes the colours, as does alteration of the genes. Some of the relations are the following:

D. The 'sun-red' type requires exposure to the sun for production of the red colour. Parts protected from the sun are green. In the 'green' types, on the other hand, subjection to the sun does not cause the production of red colour. Thus the difference between red and green plants is due in some cases to diversity of genes, as when 'sun-red' and 'green' types are both grown in the sun. In other cases the difference between red and green plants is due to environmental difference, as when 'sun-red' plants grown in the sun are compared with those of the same type grown in the shade.

The plants of the 'purple' type do not depend on exposure to the sun for their colour; they are purplish in colour whether grown in sun or shade.

The degree of colour produced by exposure to the sun depends on what genes are present. In the typical 'sun-red' variety, exposure to the sun causes a red colour widely distributed on the plant. In the 'dilute sun-red', exposure to the sun under similar conditions causes only a little red, at the bottom and tips of the leaves, while in the 'green' type no red appears.

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E. The nature of the soil affects the colour. 'Dilute sun-red' grown in poor soil and subjected to the sun has almost all parts red; in good soil, with the same relation to the sun, it has very little red. The 'green' and 'brown' types are not influenced in their colour by the nature of the soil.

F. Certain particular chemicals in the soil affect the colour. Presence of much nitrogenous matter tends to suppress the red; if little is present the red colour is marked.

G. Storage of carbohydrates in the leaves of the colour-producing varieties causes increase of the red colour. The amount of carbohydrate in the leaves may be increased by experimental procedures, as by removing the growing ears, or by bending a leaf so as to break the conducting vessels; the leaves thereupon become red in the parts with increased carbohydrate. But this effect is not produced in the 'green' types; they do not produce the red colour even in presence of stored carbohydrates.

It appears clear, therefore, that in maize different genes cause the different varieties to have different metabolic processes, different chemical reactions, some of which cause the production of colours, while others do not. Also, diverse environmental conditions likewise cause changes in these metabolic processes, inducing colour production in some cases. Whether colour occurs, and its type and amount, depend on interaction of genetic and environmental conditions.

Another instructive case of the interaction of genes with environmental conditions is furnished by the conditions determining the number of facets in the compound eye of *Drosophila*.⁵ In the normal eye there are present about 800 facets. In certain of the flies a gene at locus 57 in the X-chromosome is so modified as to cause a great reduction in the number of fully developed facets. In this condition, known as Bar-eye, there are only about 80 fully developed facets: these form a 'bar' across the eye (Figs. 9 and 10). This Bar-eye condition is dominant; the number of facets is reduced even though one of the two genes of the pair is normal. We may call the modified gene that causes the reduction in the number of facets the Bar gene.

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The number of fully formed facets, it is found, depends on whether there is present but one or two of the Bar genes, and also on whether there is present in addition a normal gene. In the males (having of course but one X), the presence of the Bar gene reduces the number of normal facets to about 90. In the female, if both the X's contain a Bar gene, the number of facets is about 65. If the female is heterozygotic, so that but one of her X's contains the Bar gene, while the other is normal, the mean number of facets is about 358. Finally, in either male or female, if no Bar gene is present, the number of facets is about 800.

Later it was discovered that this Bar gene is sometimes modified in a different way, so as to cause a less marked reduction in the number of facets. This modification is known as infra-Bar. A female containing but one of these infra-Bar genes has about 716 facets; if she contains two she has about 348.

Again, by an extraordinary process, almost or quite unique in known genetics, in some cases two of the Bar genes get united by crossing-over into one X-chromosome. This condition is known as double Bar. When both of the chromosomes carry this double Bar, the number of facets is but about 25. If one carries double Bar, the other single Bar, the number of facets is about 36.

Thus the number of facets in the eye depends in many ways on the number and conditions of the genes present. This may be shown in the following diagram, representing the conditions in the two X (or Y) chromosomes of any individual, with the corresponding numbers of eye facets present. In this diagram

+ = the normal, unmodified X-chromosome

Y = the Y-chromosome of the male

B = the Bar gene

iB = the infra-Bar gene

BB = the double Bar condition (two Bar genes
in one chromosome)

Chr. 1:	+	iB	B	iB	B	iB	B	BB	BB	BB	BB
Chr. 2:	+	+	+	iB	Y	B	B	+	iB	B	BB
Facets	800	716	358	348	98	73	65	45	42	36	25

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All these various conditions are inherited as unit-difference, sex-linked characters; they are typical hereditary conditions.

But it is found further that the number of facets in most of these conditions depends also on the temperature to which the developing animals are subjected. The numbers given above are those observed by investigators working with fruit-flies cultivated at ordinary, not precisely controlled, temperatures. If different sets of flies are kept at different temperatures, it is found that high temperatures reduce the number of facets in the individuals that carry the Bar genes, though not in the normal individuals. Krafka found the following mean numbers of facets in the various gene conditions, at different temperatures:

Temperature, Degrees	Bar Females B-B	Bar Males B-Y	Double Bar Females BB-BB	Double Bar Males BB-Y
15	214	270	51	61
20	122	161	33	37
25	81	121	25	28
30 or 31	40	74	15	14

Thus the number of eye facets depends both on the genes and on the temperature. The number 61 may be produced either by a double Bar Male (BB-Y) at 15 degrees or by a Bar Female (B-B) at between 25 and 30 degrees. Changing either the genes or the temperature will change the number of facets.

Similar situations occur in vertebrates; one of these may be described briefly. The spotted salamander, *Salamandra maculosa*, is largely black in colour, with spots or stripes of yellow.⁶ The amount of yellow differs in different cases, so that on the whole some specimens are lighter, some darker. In the lighter individuals the yellow spots tend to run together into rows. The different grades are heritable; certain stocks are regularly darker, others lighter. If darker and lighter individuals are mated, the two conditions show Mendelian inheritance, the darker condition being dominant (Fig. 51);

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all the F₁ generation are darker, while in F₂ there are three dark to one light. The difference between the two thus depends on a difference in one gene.

But it can be shown also that the extent of colour depends on the environment. If the salamander is kept continuously for a long time (a year or two) on a light background, the yellow spots increase in size: they may run together into stripes or into large yellow areas, as in Fig. 51, B, so that the animals become much lighter. If, on the other hand, they are kept for long periods on a dark background the yellow areas decrease in size; the animals become on the whole darker. The extent of the yellow colour thus depends both on the genes and on the environment; it can be altered by appropriately changing either.

In all these cases the following general principles apply:

1. What are really inherited (passed on from parent to offspring) are the genes; that is, certain materials that in certain combinations and under certain conditions give rise to certain definite characteristics.
2. With the same original genes, different environmental conditions may induce the production of diverse characteristics.
3. Also, with the same environmental conditions, different genes may induce the production of different characteristics.
4. The same difference in characteristics that is in one case produced by diversity of genes is in other cases produced by diversity of environment.

There can be little doubt that these general statements apply to many characteristics in man. Some combinations of human genes form an individual that is a much better culture medium for the bacteria of tuberculosis than are others. A person who gets such a combination of genes will develop tuberculosis, if he lives in a region in which the germs of that disease are abundant; while another person, with a different set of genes, will not be subject to tuberculosis, even though living under the same conditions. And the person with the genes that make him susceptible to tuberculosis will not have the disease if he prevents infection by the tubercle bacillus.

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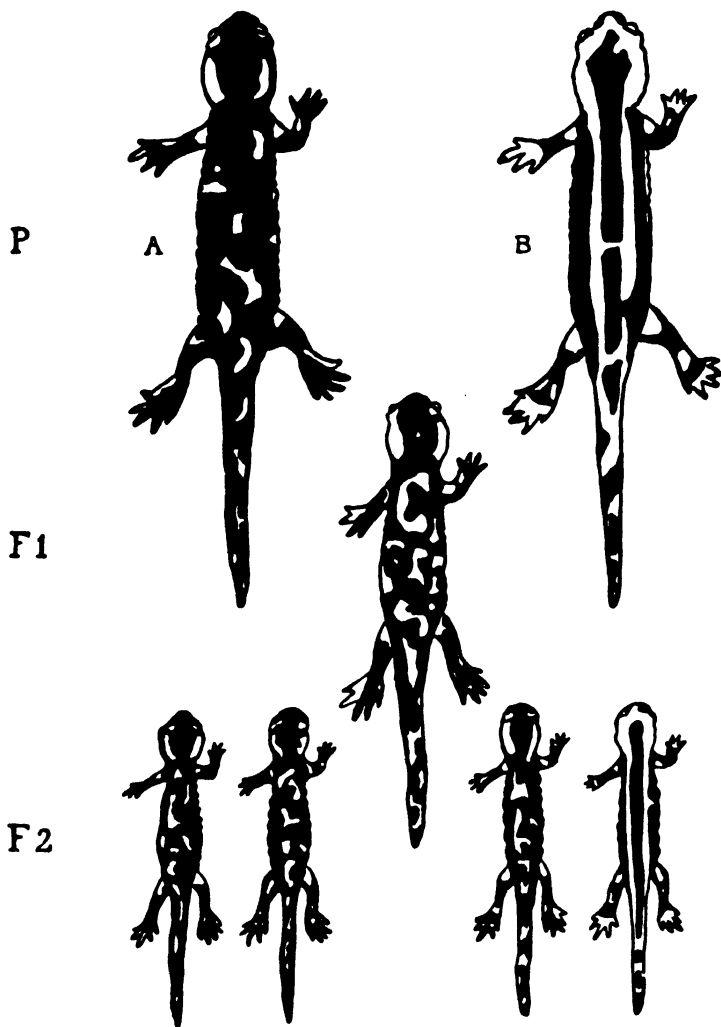


FIG. 51.—Mating of darker (A) and lighter (B) individuals of *Salamandra maculosa*, with the F1 and F2 generations: in the latter 3 dark to 1 light. After Kammerer (1913). (In the originals the light areas are yellow.)

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In relation to such susceptibility there are doubtless a great number of grades, dependent on just what combination of genes is present. Some are extremely susceptible, others less so but still prone to the disease, and so on, up to individuals whose gene combinations are such as to give them natural immunity to tuberculosis.

What then shall be answered when it is asked whether tuberculosis is hereditary or not? One can only say that some gene combinations predispose to it more than others, so that a hereditary factor is involved. But also there is a necessary environmental factor; it is the interrelation of the two sets of factors that determines whether the individual shall be afflicted with the disease.

Similar considerations apply to any other disease, acute or chronic. Certain combinations of genes are doubtless more readily attacked by plague, by smallpox, by typhoid, by pneumonia, than others, just as certain genetic constitutions yield more readily to extremes of temperature, to exposure to the elements, to unfit food. There is no affair of life in which the gene combination borne by the individual does not play a part. But the environment too plays a part, often an overwhelmingly important part.

The relative rôle played by genes on the one hand, and by environment on the other, is not the same for all characteristics. Differences in certain features of the organism are mainly due to differences in the genes of which they are composed. In other characteristics, differences are due mainly to environmental diversities. There are all sorts of intermediate conditions between these extremes. We may pass in review a number of different types of characters from this point of view.

Most of the diversities in obvious physical features in most animals are the result of differences in the genes, so that they are mainly matters of inheritance rather than of environment. In *Drosophila* the forms of the parts of the body, of the legs and wings, the distribution of bristles, the venation of the wings, the colours of body and eyes, are all changeable

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through the action of diverse genes, but diversities in these features due to environmental action are relatively rare. This is the case also for such characters in the vertebrates, including man. Most of the physical characters of human beings—form of their features, complexion, colour of hair, form of limbs, and the like, as well as sex—are settled mainly while the child is carried in the mother's body, when the differences in environment are very slight. The diversities between individuals in these respects are almost entirely—though not quite entirely—the result of differences in the genes; they are matters mainly of inheritance. This is demonstrated by what we find in twins. The one-egg twins, having the same genes, are usually closely alike in their physical peculiarities, while the twins derived from different eggs, and so having different genes, are much more diverse with respect to such physical characteristics. At times, of course, one-egg twins become diverse through accidents or diseases which affect one and not the other. But physical diversities in twins due to genetic differences are much more frequent than those due to environmental differences.

In some organisms the gross physical features are readily altered by environmental diversities, so that differences between individuals resulting from the different conditions under which they have lived are common. Such is the case with the habit of growth in higher plants; trees and other plants grown under different conditions are very different in form. In some of the lower animals, such as the hydroids, a similar situation is found.

It is obvious that the details of behaviour are in a high degree under the influence of environmental conditions. The particular acts performed at given moments in any given organism are determined almost entirely by the conditions under which it finds itself. Yet organisms of different genetic constitution behave very differently under effectively the same conditions, and the general pattern of the behaviour of organisms may be largely determined by the genetic constitution.

*Genes and Environment in relation to Mental
Characteristics. Evidence from Twins*

The relative rôles of heredity and environment are of special interest in man, particularly in relation to the characteristics that influence behaviour. For the study of these matters man is the most favourable organism that exists, although for most other relations in genetics he is a singularly unfavourable object of study. In man it is possible to make detailed studies of temperament, mentality, character, a group of characteristics hardly open to examination in other organisms. Furthermore, there occur in man 'identical' or one-egg twins, individuals having the same set of genes, the same genetic constitution throughout.⁷ And for comparison with these there occur fraternal twins: two individuals of the same parentage, the same age and living under the same environment, but developed from two separately formed eggs and thus having to some extent different sets of genes. By comparing these two kinds of twins with one another and with unrelated individuals, opportunity is presented for comparisons of the results of similarities and diversities in genetic constitutions with those of similarities and diversities in environmental influences.

As seen in Chapter 8, the twins derived from a single egg are as a rule very closely alike in most physical respects; it is this that has caused them to be called identical twins. In some cases, however, the two differ in certain physical characteristics. There appear to be two categories of causes for these differences. First, there are physical differences that result from the way in which the separation of the twins occurred. Separation of the single egg into two does not occur in the first stages of development, as by division of the one-cell stage into two. On the contrary, it occurs much later, when many cells are present and the differentiation of bodily parts has begun, and it occurs at different ages in different cases. There is reason to believe that when an equal division occurs at a rather early stage, before the right and left halves of the body

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have begun to show their characteristic diversity, the two twins produced are closely alike in their physical features. At a later period the right and left halves of the embryo have begun to differ, in the way that results as a rule in the greater strength and development of the right hand and arm. At such a stage, the embryo may divide into right and left halves, with results as follows. Of the two embryos so produced, one will have a right limb that is already somewhat advanced in development, while the left limb, formed at the plane of separation, must begin anew. The other embryo will be in the reverse situation; it will have a left limb already somewhat advanced in development, but the right limb, formed at the plane of separation, must begin anew. In each case the more advanced limb retains its advantage and becomes the one that after birth is strongest and most used. The result necessarily is that one of the twins remains right-handed, while the other becomes left-handed. This situation is not uncommonly found in identical twins. Similar differences in other unsymmetrical parts may be produced in the same way: for example in the whorls of hair on the head. In such respects the two members of a pair often show 'mirror-imaging', presumably due in each case to the fact that the original embryo had already become a little unsymmetrical before division occurred.

From this same situation another condition often observed is believed to result. In the embryo before division, one side (usually the right) will be a little in advance of the other. After division, the twin derived from the right half continues to retain this advantage, so that it may be more vigorous than the one derived from the left half. Such differences in vigour are not rare in twins. Apparently they may be accompanied by a psychological difference; the more vigorous twin assumes the leadership in their lives together. This reacts further on temperament and character. How far psychological and temperamental differences so produced may go is uncertain.

It appears that in some cases division of an embryo may be unequal, so that for this reason also one twin may be more vigorous than the other, with resulting psychological differences.

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Diversities produced in the ways above described are different in origin and type from those commonly called environmental. Under the latter term are commonly grouped diversities resulting from the different conditions under which individuals have lived. Since the extent to which differences due to the time and method of division may go, and the kind of characteristics that they may affect are uncertain, it is often not possible to distinguish these certainly from diversities due to differences of environment after division has occurred.

Belonging to one or the other class, there are sometimes marked differences in the physical characteristics of one-egg twins. Komai and Fukuoka⁸ have described two fifteen-year-old Japanese boys that are obviously one-egg twins; they show the usual close resemblance in form, features, colouring, and the like. But they now differ greatly in size. One is taller by 14·8 centimetres, or about 6 inches, and his weight is greater by 10·4 kilograms, or about 23 pounds. The two were at first of the same size, the difference gradually arising during growth. The smaller of the twins is affected by diabetes insipidus; this is probably connected with his decreased growth. The larger twin is right-handed, the smaller left-handed. Whether the difference in health and growth is in some way connected with what occurred at division of the egg is uncertain.

A comparable case is described by Siemens.⁹ Two sisters, clearly one-egg twins, were as usual nearly identical in most of their physical characteristics till the age of 10. At this time one of them became affected with a severe lateral curvature of the spine, and from this time their development was very different; at 16 the healthy twin was 4·8 inches taller than the other. The origin of the defect that produced curvature of the spine and changed development is unknown.

Identical twins that have lived together sometimes show considerable psychological differences. Newman has made extensive psychological tests on fifty pairs of identical or one-egg twins, and, for comparison with these, on fifty pairs of fraternal twins. The results of these examinations have not

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yet been published in full, but certain data from them have been published. By the Stanford-Binet tests, the intelligence quotients (IQ) and the 'mental age' were determined for the two sets. The two classes of twins are best compared by the differences between the scores made by the two members of each pair. These differences were as follows:

	Mean difference in Mental Age	Mean difference in Intelligence Quotient
Identical Twins 50 Pairs	} 8 years 4 mo.	5.3 points
Fraternal Twins 50 Pairs		9.9 points

Thus the average difference between fraternal twins, having somewhat diverse genetic constitutions, is nearly twice as great as that between identical twins, in which the genetic constitutions are alike.

But it is important that the identical twins that have lived together also showed differences between members of the pairs. In different pairs there was much variation in the amount of diversity. Of the 50 pairs there were five in which the two members gave identical scores in the intelligence tests; the difference of their scores was 0. At the other end of the scale were five pairs that showed respectively the following differences (points in the Stanford-Binet scale) between the two members: 12.6, 12.9, 13.0, 13.9, 16.0.

All these five differences are considerably greater than the average difference between the genetically unlike fraternal twins. It is clear that in some cases even identical twins living together differ much in mentality. Whether the differences are the result of original diversities consequent on the method of division of the egg, or have been produced in some way by different experiences of the two, is not known.

For comparisons as to the relative effects of genetic and environmental diversities on mental characteristics, valuable data have been obtained from the examination of identical twins that have lived apart under different environments. The first case of this kind was carefully studied by Muller,

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and nine pairs have since been fully examined by Newman.¹⁰ In each of these ten cases the twins were separated in infancy, being adopted into different families; they have then lived to adult life under diverse conditions and influences. In addition to careful observations as to character and temperament, they were subjected to psychological and temperamental tests by the best standardized methods available.

The type of results reached by these studies will best be appreciated by first looking at the detailed resemblances and differences in some particular cases. In the first such study, by Muller, there were twin sisters that had been separated when two weeks old, and that did not see each other till they reached the age of 18; from that time until the age of 30 they lived apart more than nine-tenths of the time. Physically they showed the extreme similarity in characteristics that is usual in identical twins. Both 'have always been intellectually active', 'both have been extremely energetic, capable and popular, and they have been prominent in all sorts of club work in their respective communities' (Muller). 'Both have had two or three attacks of tuberculosis, almost simultaneously'. The usual intelligence tests gave results very closely alike for the two twins. But 'the non-intellectual tests—of motor reaction time, association time, "will temperament", emotions and social attitudes—gave results in striking contrast with those of the intelligence tests, in that the twins gave markedly different scores in all these tests'. The differences were on the average greater than those between two individuals taken at random, and seemed 'to be correlated with salient differences in their past experiences and habits of life'.

Thus this first study of such a case indicated that the different environments and experiences of the two individuals had produced a large effect on temperament, emotions, and social attitudes, but had had little effect on such matters as are tested by intelligence tests.

An illuminating contrast with these results is given by the first pair studied by Newman. The twin sisters ('O' and 'A') were born in London and were separated at the age of 18 months. One lived in Ontario, Canada, the other in London.

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Their environments were very different. When they were tested, this pair gave differences in those tests in which Muller's pair gave similarities, and gave similarities in those tests in which Muller's pair gave differences. Newman says: 'The twins dealt with in this paper are very different in mental capacity'. But they showed great similarity in their manifestations of will and temperament, and in their emotional reactions. So this pair of twins shows that differences in the experiences undergone affect deeply the individual's mental traits: his performance in matters brought out by intelligence tests.

Important points were brought out in the study of Newman's second pair, twin sisters ('E' and 'G'). The two had received very different educations; one had attended school seven years longer than the other. Newman summarizes as follows the results of his study of these:

'These twins, remarkably similar after being separated at 18 months of age and unknown to each other for 19 years, have been profoundly modified by the very different educational careers. In every test of mental capacity, whether of so-called native ability or of achievement, 'G', the more highly educated twin, has distinctly the superior mind. Obviously mental training improves the ability of an individual to score well in any sort of test'. But further, 'in contrast with the great difference in mental power stands the fact that in all the tests of emotional traits and of temperament the twins gave the impression of being remarkably and unusually similar'. Here came out the effect of their identity of genes.

Newman's third pair revealed certain other facts of importance. These were two young men ('C' and 'O'), separated at two months of age. One had lived mainly in the city while the other had lived in the country. They were examined after reaching the age of 23. The results are summarized by Newman as follows:

'In native ability they seem to be nearly identical. The one outstanding difference is in their general personalities. 'C' (who had lived in the city) impresses one as more dignified, more reserved, more self-contained, more unafraid, more

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experienced, and less friendly. He seldom smiles, has a more serious expression about the brows, eyes and mouth. He stands more erectly with chin held in and brows drawn down somewhat over his eyes. 'O' (the other twin) is the opposite in all these respects. He is the more typical country boy, laughs readily, and is not on his dignity at all.' Newman asserts emphatically that 'the personalities of the boys were utterly different'.

Thus through the study of these first four pairs examined, of identical twins that have lived apart, it became clear that such twins may differ in many ways. It appeared that the different environments and experiences of the individuals may have a large effect on mental and temperamental characteristics. The effects were different in different cases: in some cases the twins are alike in intelligence but differ temperamentally; in other cases they are alike in temperament and emotions, but differ in mentality. In other cases the marked difference is best expressed rather vaguely as a diversity in 'personality'.

The general impression given by study of these first four cases has been confirmed by Newman's study of six other pairs of identical twins that have lived apart. The nine cases examined by Newman were treated by uniform methods, so that they may be compared in such a way as to bring out general relations.

The intelligence quotients for the two members of the nine pairs are as follows (Stanford-Binet scores in points):

<i>Pair</i>	<i>IQ</i>	<i>Difference</i>
I	97 and 85	12
II	67 and 78	11
III	99 and 101	2
IV	106 and 88	18
V	93 and 89	4
VI	102 and 94	8
VII	106 and 105	1
VIII	92 and 77	15
IX	102 and 96	6

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The mean difference in intelligence quotient for these nine pairs of identical twins that have lived apart is 8·6. This is considerably greater than the mean for identical twins that have lived together, which was 5·3. So far as it goes it indicates that difference of environment has a considerable effect in increasing the mental difference between twins. In cases I, II, IV and VIII, the difference between the twins was very marked, but is similar to the differences between the five extreme cases of identical twins that had lived together (12·6, 12·9, 13·0, 13·9, 16·0). This emphasizes the fact that it is not possible to be certain what differences are due to something that happened at the division of the egg, and what are due to later environmental differences. The mean difference between identical twins that have lived apart (8·6) is nearly the same as that for fraternal twins that have lived together (9·9).

In addition to the studies of intelligence, Muller and Newman made extensive examinations designed to test other features of personality. One set was designed to test will and temperament, to distinguish the mentally quick and slow, the deliberate and careful as compared with the hasty and careless, the aggressive and forceful or the opposite, and the like. Another type of examination is designed to test emotional peculiarities: likes and dislikes, feelings of right and wrong, and so on. The results of such tests are not readily expressible by a numerical score, such as is employed for the intelligence tests. It will be worth while, however, to attempt a tabulation in general terms of the results of the tests in the three categories for the 10 cases of identical twins that have lived apart. The first case (M) is that of Muller; the others are the nine cases of Newman:

	<i>Intelligence</i>	<i>Will-Temperament</i>	<i>Emotions</i>
M	Closely alike	Very different	Different
N I	Very diverse	Alike	Alike
II	Very diverse	Closely alike	Closely alike
III	Closely alike	Closely alike	Very different
IV	Extremely diverse	Very different	Rather alike
V	Closely alike	Closely alike	Closely alike

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	<i>Intelligence</i>	<i>Will-Temperament</i>	<i>Emotions</i>
VI	Rather alike	Rather alike	Rather alike
VII	Closely alike	Somewhat different	Somewhat different
VIII	Very different	Considerably different	Somewhat different
IX	Much alike	Closely alike	Considerably different

Thus the general picture is that identical twins that have lived apart show many different combinations of likeness and unlikeness with respect to intelligence, temperament and emotional characteristics. There are cases in which the two are closely alike in all three categories (V and VI), cases in which the twins are distinctly diverse in all three categories (VIII), and cases in which they are alike in two categories and diverse in the third, or alike in one category and diverse in the other two.

On the whole, it is clear that other things, beside genetic constitution, play important rôles in determining mentality, temperament and emotional traits. The principal difficulty in interpreting the results lies in the uncertainty as to how much is the result of the manner in which division of the egg occurred, and how much is due to later environmental differences. Both certainly play a rôle. For these types of characteristics it appears probable that, of the two, the later environmental differences play the greater rôle. It is further clear that genetic resemblances and differences play a very large rôle in mentality, temperament and emotional traits.

It is to be noted that in all this study, the general environment of the twins was much alike in all cases. None of them lived in different civilizations, or at different epochs in cultural development. How great a diversity in the characteristics studied could be made by such differences remains uncertain.

It is further to be noted that the tests to which the twins were subjected were designed to bring out rather permanent personal traits, as distinguished from mental content and habitudes. The behaviour of human beings depends very largely upon acquired mental content, upon knowledge, and

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upon habitudes, and these things are in a high degree dependent on the conditions under which the individuals live and the experiences to which they are subjected.

In general, it is clear that in a human population there are great numbers of different types of individuals that are diverse because their genetic constitutions are diverse. In consequence of this they differ in their capabilities, in their tastes, in their tendencies toward any particular line of action. But all these classes, so far as they do not fall in the seriously defective groups, have marked powers of adjusting themselves to many different conditions and of following many different lines of action, depending on the conditions in which they live.

In no other organism than man is so full an analysis possible of the relative rôles of genetic constitution and environment in determining the mental and temperamental characteristics, for in no other organism are these characteristics highly developed.

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I I

EFFECTS OF MIXING DIVERSE ORGANISMS. HYBRIDIZATION

1. Incompatibility of Paternal and Maternal Germ Cells in Development

In the chapters up to this point we have described what may be considered the normal operation of the genetic system and the results of this operation. We now examine certain features that may be called abnormal, resulting from the crossing of very dissimilar organisms.

Union of germ cells to produce offspring commonly occurs only in the case of closely related organisms having germ cells and genetic systems that are closely alike. Very diverse organisms, such as molluscs and echinoderms, or starfish and sea urchins, differing greatly in their chromosomes or in other features of the germ cells, commonly do not cross. When the sperms of one such type are brought into contact with the ova of another, the sperms do not enter the ova; there is no fertilization.

A method of inducing cross-fertilization between certain very diverse marine organisms was discovered by J. Loeb.¹ By putting certain chemicals in the sea water, he found that the sperms from one type could be caused to enter the ova of very different types, bringing about development. In this way he induced fertilization of the ova of the sea urchin by sperms of starfish, holothurians, and even molluscs and annelids. Later such work was greatly extended; many other distant crosses were made.

It turned out that, in such crosses between very diverse organisms, the development of the egg produced offspring that were not intermediate between the two parental types,

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but were like the mother only. Sea urchin ova fertilized by starfish, holothurians, molluscs or annelids, gave rise to typical sea urchin young, showing no influence of the male parent.

What is the cause for this result? Why are the chromosomes and genes of the sperm without effect on the characteristics of the offspring?

A careful cytological examination by Kupelwieser (1909)² of developing sea urchin eggs that had been fertilized by mollusc sperm showed that the chromosomes of the sperm do not enlarge, as is usual after fertilization. They do not unite with the chromosomes of the ovum, do not divide, take no part in development, and ultimately die in the early stages of development (Fig. 52, A). This then is the explanation of the fact that the offspring of the cross show none of the characteristics of the male parent. The paternal chromosomes play no rôle in development and therefore do not affect the characteristics. What the sperms do is merely to initiate development; for the rest, development is essentially parthenogenesis; it is development of the ovum alone.

In such cases the sperm are unable to live and develop in the cytoplasm of a very diverse organism; there is incompatibility between the two.

In other crosses between very diverse types, essentially the same thing occurs, although there are differences in details. When the sea urchin ovum is fertilized by annelid sperm, the sperm nucleus unites in the usual way with the nucleus of the ovum, so that the two form a single nucleus. But before this nucleus divides, it ejects the annelid chromosomes, which are then lost in the cytoplasm (Fig. 52, B). The egg continues development with only the sea urchin chromosomes, producing only sea urchin young.

In such cases there is, seemingly, incompatibility between the two types of chromosomes; those of one type are cast out and destroyed.

When the parents are somewhat less diverse, the processes are less striking in appearance, though the ultimate result is the same. When sea urchin ova are fertilized by sperms of the

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crinoid (both being echinoderms), the sperm nucleus unites with the egg nucleus, and its chromosomes are not ejected

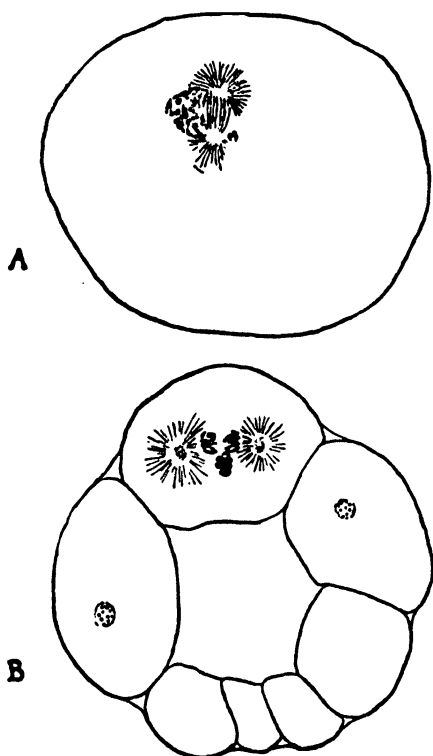


FIG. 52.—A, Sea urchin egg fertilized by mollusc sperm. Spindle forming for the first division of the large egg nucleus. The sperm nucleus a small black mass at the right of the lower end of the spindle; it takes no part in the division. Redrawn from Kupelwieser (1909).

B, Section of a 16-cell stage of a sea urchin egg that was fertilized by annelid sperm. In the large upper cell the sperm chromosomes are separated as a dark mass from the dividing egg chromosomes. Redrawn from Kupelwieser (1912).

nor destroyed (at least not in the early stages of development).³ But the chromosomes from the crinoid have no visible effect on the method of development, though they

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cause the offspring to die in early stages. So far as they develop the young are exclusively sea urchin in type.

When the parents are still more nearly related, as when different genera or species of sea urchins are crossed, varied results are produced. Sometimes the offspring are like the mother species exclusively. Sometimes they are like the mother almost completely, but show a few characteristics of the father. And sometimes they are intermediate between the two parental species. These different results occur in different cases when the same two species are crossed.⁴

In judging of these results, certain considerations must be kept in mind. Such crosses have been made mainly in sea urchins. These do not as a rule develop in captivity beyond the free swimming larval stage, so that the characteristics observed are those of the larvae only. In *Sphaerechinus* the larva has a latticed skeleton (Fig. 53, A), while in *Paracentrotus* the skeleton is composed of simple rods (Fig. 53, B). If *Sphaerechinus* ova are fertilized by *Paracentrotus*, in some cases all the progeny have a lattice skeleton like that of the mother; in other cases the skeleton is intermediate between that of the two parents (Fig. 53, C).

Why are such diverse results produced in different cases of the same cross? The cause for this was discovered by Herbst. Under certain conditions the sea urchin ovum begins development before the sperm enters. This can be induced by treatment with certain chemicals. When such ova as have begun to develop, and are nearly ready to divide, are fertilized, the larvae produced are those of the mother species only. But if fertilization occurs before the egg nucleus has enlarged in preparation for division, the larvae produced are intermediate in character between those of the two parents.

Cytological examination showed that in the cases in which the egg nucleus had begun the developmental processes before fertilization occurred, the sperm chromosomes lag behind those from the egg nucleus. They do not succeed in uniting with egg chromosomes into a single nucleus. In cell division the sperm chromosomes are seen lying to one side, in a less advanced condition than the egg chromosomes (Fig. 54).

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They never catch up in the developmental processes. They are irregularly distributed to the various cells produced; they become abnormal and finally some or all of them die. In such cases the larvae produced are either completely maternal in their characteristics (Fig. 53, D), or with a slight admixture of paternal characteristics. The different results seemingly depend on how far behind the paternal chromosomes are, and whether they are finally completely eliminated.

In case, however, fertilization occurs before the egg nucleus has begun to enlarge for development, the paternal and maternal chromosomes take equal parts in development, and the larvae produced are therefore intermediate.

Similar conditions have been shown by Tennent and others to prevail in crosses between a considerable number of different species of sea urchins. A case of perhaps special interest has been described by Baltzer.⁵ When the ova of a species of *Paracentrotus* are fertilized by sperm of a species of *Sphaerechinus*, the chromosomes from the sperm are almost entirely eliminated (apparently four out of eighteen persist). The larvae produced are almost completely maternal in character. On the other hand, in the reverse cross, when the ova of *Sphaerechinus* are fertilized by sperm of *Paracentrotus*, the sperm chromosomes are not eliminated, but take part in development, and the larvae produced are intermediate. It appears that the *Paracentrotus* chromosomes can operate in the cytoplasm of *Sphaerechinus*, but most of the *Sphaerechinus* chromosomes cannot operate in the cytoplasm of *Paracentrotus*.

Thus it is clear that in different cases there are various degrees of antagonism between the chromosomes of one organism and the cytoplasm (or the chromosomes) of another. The results of crossing depend on the degree of this antagonism.

Often the chromosomes of two species differ in number and size. Frequently it is found that in such cases they do not work well together in development. The cross-fertilized egg begins to develop, but soon development ceases and the embryo dies. In Moenkhaus' work on crossing two genera of

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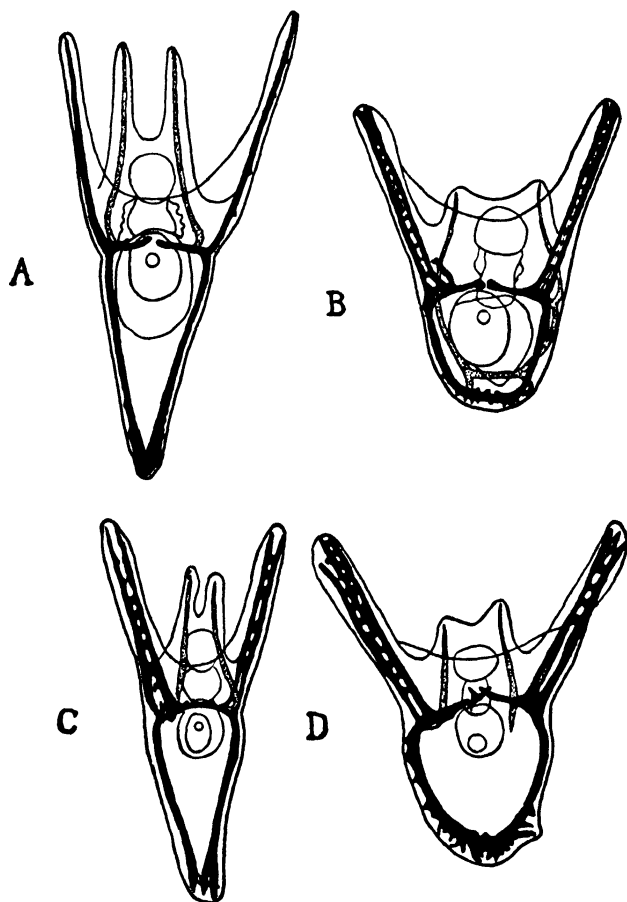


FIG. 53.—Results of crossing different genera of sea urchins. A and B are the larval skeletons of the parents, A, *Paracentrotus*, B, *Sphaerechinus*.

C, Normal hybrid, intermediate between the two parents. D, Hybrid that is entirely maternal in type, resulting from the failure of the sperm chromosomes to take part in development. After Herbst (1925).

fish, *Fundulus* and *Menidia*,⁶ it was found that the chromosomes of the two differ greatly (Fig. 16, in Chapter 2). The

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egg containing the two kinds of chromosomes begins to develop, but soon development takes an abnormal course and after a time ceases. Many cases of this type have been fully studied; they are common.

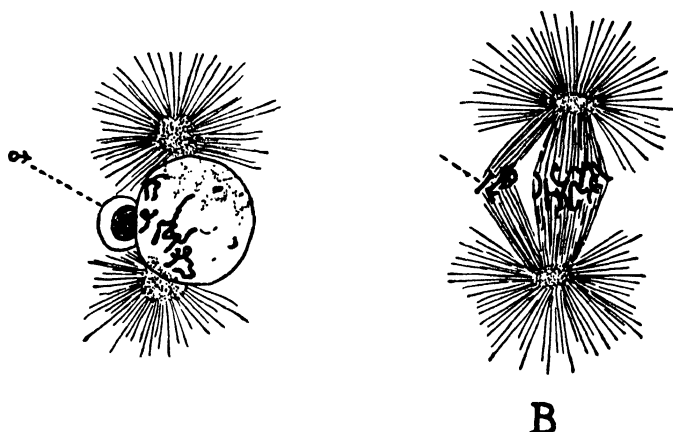


FIG. 54.—Two figures showing the lagging behind of the male nucleus and chromosomes in eggs of *Sphaerechinus* fertilized by sperm of *Paracentrotus*, after the egg nucleus has begun to enlarge for development. In A, the egg nucleus is enlarged and in it the chromosomes have appeared, while the sperm nucleus (to the left) is small and without nuclei. In B, the egg chromosomes, at the right, are approaching division, while the sperm chromosomes, to the left, form a small separate group less advanced in development. See text. After Herbst (1909).

2. Incompatibility of Paternal and Maternal Chromosomes in the Formation of the Germ Cells of Hybrids

In the cases thus far described, the chromosomes of the father show themselves incompatible with the chromosomes or cytoplasm of the mother, so that either the parental chromosomes are eliminated, or development becomes abnormal and ceases.

In another class of hybrids the incompatibility of paternal and maternal chromosomes does not show itself until the hybrids form germ cells for the next generation. The indivi-

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dual hybrid produced by germ cells from different species develops well, may even show hybrid vigour, becomes adult. The two kinds of chromosomes work together well in the development of the individual.

But when in this hybrid individual the period arrives for the two kinds of chromosomes to conjugate in forming germ cells, the incompatibility shows itself. In the intimate union of chromosomes at conjugation, the two types of chromosomes injure or destroy one another, so that no germ cells are found. The hybrid individuals are therefore sterile, or partly sterile.

Sterility in hybrids is very common. A typical example is the mule (Fig. 55). Of the two parents, the horse has 37 or 38 large chromosomes,⁷ the ass 65 or 66 small ones. These work well together in development: the mule is perhaps more vigorous than either parent. But when germ cell formation begins in the mule, the two kinds of chromosomes at the time of conjugation partly or entirely destroy one another (Fig. 55, B). No functional germ cells are formed.

In other cases the sterility of the hybrids is not complete. Some of the chromosomes of the two species refuse to conjugate, while others do conjugate. The number that conjugate successfully varies in different germ cells even of the same hybrid individual. Some of the chromosomes are injured or eliminated. Thus many of the germ cells formed are imperfect; many die. The production of a large proportion of imperfect germ cells is one of the commonest features of hybrids. Some of the germ cells, however, may live; these are presumably the ones in which the chromosomes have been least injured. Such germ cells may function; by their union the hybrids may produce a few offspring. Such offspring may be abnormal or imperfect, or some of them may develop normally.

For example, Federley⁸ crossed two species of butterflies, *Pygaera curtula*, which has 58 chromosomes, and *Pygaera anchoreta*, which has 60 chromosomes. The hybrids (F₁) produced are normal and have 59 chromosomes; 29 from *P. curtula*, 30 from *P. anchoreta*. In forming germ cells (sperms)

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in the hybrids, the *curtula* and *anchoreta* chromosomes refuse to conjugate; or a few conjugate, the rest do not. The result is that there is no reducing division; in the final germ cells the full number of 59 chromosomes is present. Add to this the fact that in attempting to conjugate some of the chromosomes

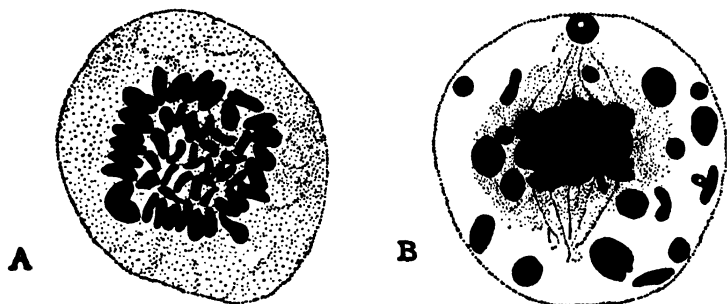


FIG. 55.—Chromosomes of the mule in germ cell formation. A, Early stage in germ cell formation, showing the large chromosomes of the horse and the small chromosomes of the mule.

B, Later stage of germ cell formation. Germ cell and chromosomes degenerating; chromosomes irregularly scattered. After Wodsdalek (1916).

are injured or partly destroyed. The result is that the sperms thus produced are abnormal. Most of them will not fertilize the ova; they die without giving origin to offspring. But a very few succeed in fertilizing ova and producing a few offspring (F₂).

In another cross of butterflies studied by Federley, one species, *Pygaera pigra*, has but 46 chromosomes, while the other, *Pygaera curtula*, has 58. In the hybrids there are 23 + 29, or 52 chromosomes. In the formation of sperms by the hybrids, most of the two kinds of chromosomes refuse to conjugate. Usually some half-dozen conjugate, the rest do not. Only those that conjugate undergo the reducing division; the others divide, half of each going to each germ cell. Thus the sperms have anywhere from 44 to 52 chromosomes. On the other hand, in forming the ova, usually the 23 *pigra* chromosomes conjugate with 23 of the *curtula* chromosomes,

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leaving 6 *curtula* chromosomes that do not conjugate. Very few offspring are produced by the hybrids.

In cases in which the two parents have different numbers of chromosomes, in the hybrids only a part of the chromosomes can conjugate, as in the example just described. A well-known example of this sort is found in the plant hybrids of *Drosera rotundifolia* crossed with *Drosera longifolia*. The former species has 20 chromosomes, the latter 40. The hybrids have 30 chromosomes, 10 from *rotundifolia*, 20 from *longifolia*. In forming the germ cells of the hybrid, 10 of the *longifolia* chromosomes conjugate with the 10 from *rotundifolia*, leaving 10 *longifolia* chromosomes that do not conjugate. Some of the latter die, some divide, half going to each germ cell; some do not divide, but go entire to one germ cell or the other. Thus the germ cells vary in their chromosome numbers, from 11 to 18, in cases observed. Such germ cells with irregular numbers of chromosomes do not function properly; offspring are not produced from them.

A great number of hybrids have been studied in plants and animals. They show a great variety of conditions as to the conjugation of the chromosomes, injury or destruction of chromosomes, and partial or complete sterility of the hybrids, all resulting from various degrees of incompatibility of the chromosomes, combined with the occurrence of different numbers of chromosomes in the two species.

3. Incompatibility of Structures or Functions in the Two Species that are Crossed. Disharmonious Combinations

In many hybrids the chromosomes of the two species are able to work together, but some of the structures or functions developed in the hybrids do not operate well together. The result is that the hybrids are abnormal or imperfect; they may die in early stages of development.

As an example may be taken the hybrids between two species of fish, *Fundulus majalis* and *Fundulus heteroclitus*,⁹ studied by Newman (Fig. 56). *Fundulus majalis* is larger than *F. heteroclitus*, and has larger eggs. In these large eggs

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the circulation, after development has progressed, is more rapid than in the small heteroclitus eggs, so that the larger amount of yolk present is rapidly consumed. Thus when the young fish is ready to swim about, the yolk has been absorbed and does not interfere with swimming. In the smaller heteroclitus embryos the circulation is slower.

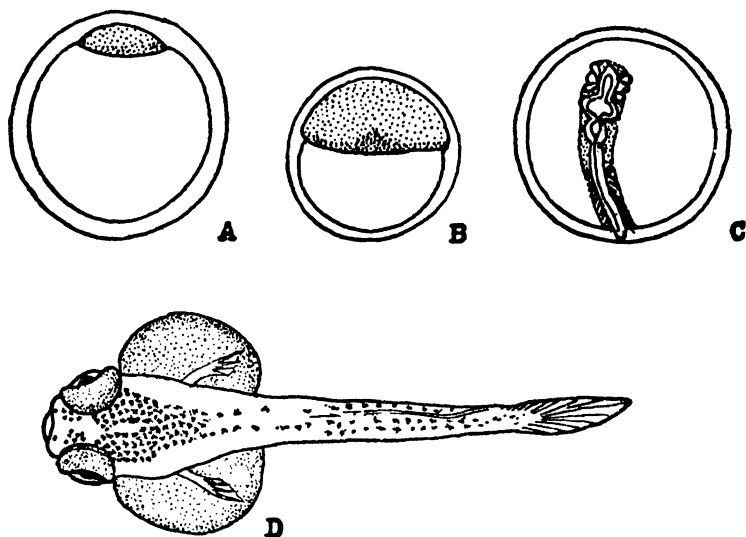


FIG. 56.—Development of a hybrid between a larger species of fish, *Fundulus majalis*, and a smaller species, *Fundulus heteroclitus*. After Newman (1908). A, egg of *Fundulus majalis*; B, egg of *Fundulus heteroclitus*; C, young hybrid developing on the large egg of *majalis*. D, young hybrid at the time that it should begin to swim about; there still remains a large mass of egg yolk, which prevents successful swimming, so that the hybrid dies.

When the large *majalis* egg is fertilized by *heteroclitus*, the young hybrid develops up to a certain stage. But in the hybrid the blood circulation is slower than in the pure *majalis*, owing to the crossing with the slower *heteroclitus*. The result is that the yolk is only slowly absorbed, so that when the young fish is ready to swim about it is still burdened with a mass of yolk (Fig. 56, D). It attempts to swim,

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but sinks to the bottom and dies. The slow circulation is incompatible with the possession of a large quantity of yolk.

In another respect the hybrids are in this case less fitted to survive than the pure species. The hybrids are less resistant to carbon dioxide than either parent species. The hybrid is a less efficient physiological organization than the parents.

There are many cases in which there is thus a lack of harmony in the development of hybrids, although it is not always so clear as in the above case to what the disharmony is due. Thus, Stockard reports that when the St. Bernard dog is crossed with the Great Dane, the hybrids develop but become partially paralysed when about three months old.

In some cases the hybrids develop to the adult condition, but harmony is lacking in the parts produced. These are examples of the formation of new combinations of genes and of characters produced by biparental reproduction, described in Chapter 12. The combinations formed may be superior to those in the parents, or they may be inferior. The latter seems to be more frequently the case when the two parent stocks are very diverse. There may then be produced varied combinations of parts of different form and size, some of them disharmonious. A considerable number of such cases are described by Stockard¹⁰ among crosses of different breeds of dogs. An example of such diverse combinations is the following. The short-legged Basset hound is crossed with the long-legged German shepherd dog. In the later descendants (F₂ generation), some have short legs, some have long legs, some have legs of intermediate length (Fig. 57). Many examples of this type are given by Stockard. Not all are clearly disadvantageous, though some seemingly are.

In an example given by Lang,¹¹ a dachshund (legs very short) is crossed with a St. Bernard having a large body and long legs. Some of the hybrids had the very short legs and also the large body, so that the body dragged on the ground (Fig. 58). Such a combination appears definitely disadvantageous.

In some cases the disharmony shows itself in the combination of diverse types of behaviour. Davenport¹² describes a cross of the White Leghorn fowl, which lays eggs continuously

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and does not brood the eggs or take care of the young, with the Brahma, which at intervals ceases to lay eggs, broods them and takes care of the young. The hybrid between the two lays eggs for a time, broods them, and takes care of the

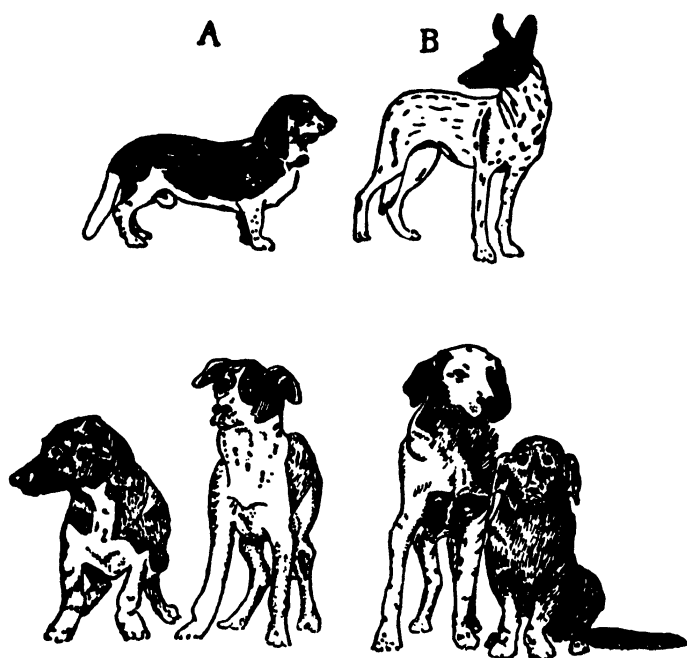


FIG. 57.—Result of a cross between long-legged and short-legged dogs. Parents above: A, Basset hound; B, German shepherd dog. Descendants (F_2) below: diverse combinations, some with long legs, some with short legs. After Stockard, *The Physical Basis of Personality* (1931).

young for a day or two. Then it abandons the young, which die from lack of care; the parent going back to the laying of eggs.

In such cases of the formation of diverse combinations of structures and functions through crossing, we approach the normal operation of biparental reproduction, described in Chapter 12. It is only in case the parents are very diverse in

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their genetic systems, or in their other structures and functions, that the results of crossing are prevailingly harmful. If the parents are not too diverse, new combinations are formed, some of which may be advantageous, others disadvantageous,

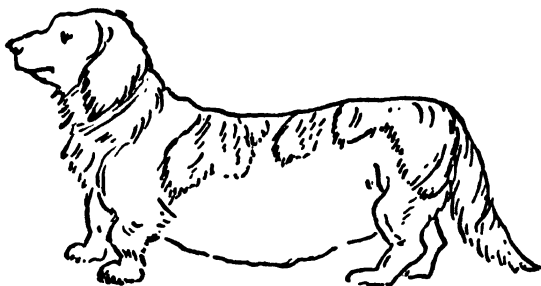


FIG. 58.—Hybrid between a Great St. Bernard dog and a Dachshund. After Lang (1914).

as set forth in Chapter 12. This appears to be the situation in crosses of the different races of man. These are not so diverse that crossing produces injuries or abnormalities. There is no evidence of incompatibility of chromosomes in the different races. And there is no incompatibility of gross structures and functions such as to cause the hybrids to die young. The hybrids and their descendants show many different combinations of the characteristics of the parent races. Some of these may be advantageous, as when 'hybrid vigour' results from the crossing of certain races. On the other hand, some of the combinations may be disadvantageous.¹³ See Chapter 12 for an account of the general principles underlying such results.

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12

GENERAL RELATIONS IN THE OPERATION OF THE GENETIC SYSTEM THROUGH THE PASSAGE OF GENERATIONS

The preceding chapters treat in detail the structure and operation of the genetic system in reproduction and inheritance. The present chapter deals with general relations which are obscured in dealing with details, relations to be observed when the units of observation are the successive generations. To present these will require recapitulation in brief of some matters already treated.

Biparental reproduction is a great process of producing new combinations of genes, and consequently new combinations of characteristics. Through it the gene combinations present in any generation are taken apart and combined anew, giving individuals having diverse characteristics from those present in the earlier generation. This is the process known as Mendelian heredity. One result of the process is that individuals of the later generation show on the average a greater similarity in characteristics to their own immediate parents than to other members of the earlier generation; also they show a greater resemblance to other descendants of those parents than to the rest of the population. These resemblances have been seized upon as of special interest, and in view of them the terms heredity and inheritance have been applied to the general process. But it is a process that produces diversities as well as similarities; it produces diversities on a grand scale.

Each individual, as we have seen, carries a definite combination of genes, which makes up its genotype or genetic

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constitution. This combination produces, under the given life conditions, a certain set of characteristics, structural and physiological. The gene combination is made up of two corresponding sets of genes, one set from the individual's mother, the other from his father. The genes are thus in pairs, the two members of each pair having analogous functions. Often one member of the pair is dominant, the other recessive.

When the individuals reproduce, this combination of genes is broken up and a new one is made by putting together half of the genes from each of the two parents (see Fig. 59). The great rule for the production of the new combination in the offspring is this: each parent gives to any individual offspring one member of each of his own pairs of genes. If the parent has a thousand pairs of genes, he gives to each of the offspring one member of each pair, a thousand single genes in all. The other parent gives also one member of each of his pairs, so that each of the offspring receives anew, from both together, the original number of pairs.

Each parent may give to the child either member of any of his pair of genes. In many cases, as we know, the two members of a pair differ in their effects on development and characteristics; commonly one is dominant, the other recessive. If we designate the two members of a pair as A and a , the child may receive either A or a , and his development and characteristics may differ accordingly. Some of the offspring receive one of the two, some the other.

Furthermore, the different pairs of genes of the same parent are in a measure independent in the way they are distributed to the offspring. If the child receives the dominant gene of one pair, he may receive either the dominant or the recessive gene of any other pair. It is true that there is a tendency (known as linkage) for two genes that are close together in either of the two parental strings of genes to go together to the same one of the offspring. But this is not absolute; genes that are side by side in the series may separate into different offspring.

Thus there are great numbers of possible different com-

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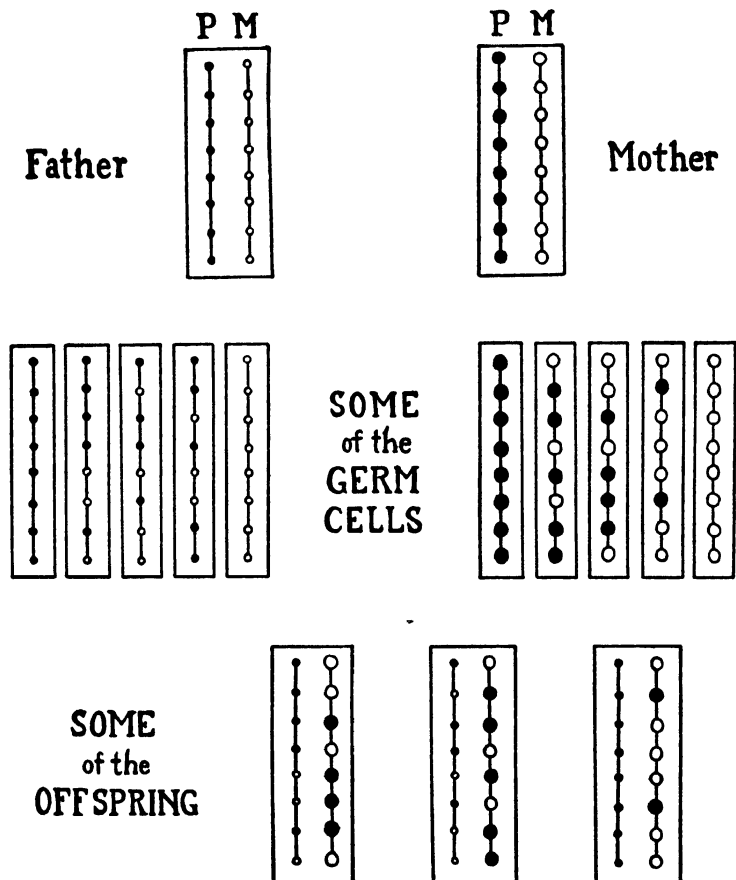


FIG. 59.—Diagram to illustrate the redistribution of genes in reproduction. In each of the two parents are two strings of genes, paternal (P), and maternal (M), represented respectively in black and white. To the germ cells the paternal and maternal genes of the parent are distributed in all possible different combinations, as indicated by combinations in the sample germ cells from each parent. Any two of the germ cell combinations may be put together to produce zygotes, as illustrated by three sample offspring. The number of diverse germ cell and zygote combinations producible is thus very great.

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binations of genes from one parent, any one of which may pass into any one of the offspring. There it may meet any one of an equally great number of possible different combinations from the other parent. The result is that the different offspring from a single pair of parents receive different combinations of genes. Thus the number of different types of offspring (with different gene combinations) that may be produced from a single pair of parents may be almost inexpressibly great; a few of such are illustrated in Fig. 59.

The characteristics that appear in the different offspring depend, we know, on what combination of genes is present. Altering a single gene may alter one or several characteristics, and may affect the developmental vigour of the entire organism. Any characteristic may be changed by alteration of one or more of many different genes. Thus the result of biparental reproduction is that the individuals produced have different characteristics. And the combinations of hereditary characteristics, like the combinations of genes, are continually changing as generations pass.

We may now pass in review some of the chief types of results that are thus produced in the passage of generations.

1. Uniparental reproduction; no change in inherited characteristics.—We may begin with the limiting cases, in which no such changes in gene combinations and in characteristics are produced at reproduction. This is the situation in vegetative reproduction from a single parent, such as occurs in many lower animals and in plants. In such reproduction each gene divides and one of its halves passes to each of the offspring, so that all the offspring receive the same combination of genes that was carried by the parent. The result is that in such reproduction the characteristics do not change as generations pass. This is the case in reproduction by fission in Protozoa and many other animals, and in reproduction by cuttings, bulbs and the like in plants. What is essentially this same process of vegetative reproduction occurs in man in the cases in which a single embryo divides to produce identical twins. The identity in characteristics of such twins is a striking illustration of the fact that in such reproduction the character-

istics are not changed. This is the usual situation in any type of reproduction from a single parent.

Of course, in such reproduction, diversities of environmental conditions may cause different characteristics to be produced in different individuals. Further, in some of the lower organisms there occur at times nuclear changes which may alter the characteristics. And genetic variations, such as are dealt with in later chapters, may occur in organisms that are multiplying by uniparental reproduction.

2. Homozygous organisms, uniform in their genes.—Even in biparental inheritance there may occur situations in which there is no change in the combinations of genes and characteristics as generations pass. This will be the case in stocks in which all the members are alike and homozygotic in all their genes.

In such a uniform and homozygotic stock, all the individuals show combinations of genes that could be represented as AAbbCCDDeeffGG, and so on. Then all the germ cells will have the same genes AbCDefG, etc. When any two of these unite they of course restore the original combination that was present in the parents, and this will continue in later generations. Thus all individuals of the stock will have the same characteristics, except in so far as modified by diversities in environment.

Such uniform and homozygotic stocks are rare in organisms bred by man, though they perhaps occur in nature. Such a stock does not remain in this uniform condition, because in time there occur genetic variations, changes in the genetic system, such as are dealt with in Chapters 13 and 14. Most of such genetic variations are harmful, so that in the severe conditions of nature the individuals in which they occur die or fail to propagate. Thus in a state of nature the uniform and homozygotic conditions may be perpetuated by this selective elimination of the individuals in which genetic change has occurred. In man and in domesticated animals this does not happen, because the weak or defective individuals resulting from genetic variations are given special care, so that they survive and propagate. Thus such organisms come to be extremely varied as to the genes that they carry.

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3. Usually there exist within species, even those living under natural conditions, several or many different stocks having different combinations of genes and of characteristics; these are known variously as stocks, races, varieties, subspecies, and the like. When two stocks having different gene combinations mate, there may appear in their descendants many different combinations of genes and of characteristics.

Thus, suppose two stocks differ in four pairs of genes, although both are homozygous. Representing by capital letters the genes that are dominant and by lower-case letters those that are recessive, the two stocks may be, for example, $AAbbCCDD$ and $aaBBCCdd$. The germ cells from these two stocks will be $AbcD$ and $aBCd$ respectively. When these unite there are produced individuals (F_1), all of which have the constitution $AaBbCcDd$; they are heterozygotic for all the four pairs of genes.

Suppose now that these individuals of F_1 interbreed. Each produces numerous different types of germ cells, having different gene combinations. From the four heterozygotic pairs there are 16 types of germ cells producible; these are: $ABCD$, $ABCd$, $ABcD$, $AbCD$, $aBCD$, $ABcd$, $AbCd$, $AbcD$, $aBcD$, $abCD$, $Abcd$, $aBcd$, $abCd$, $abcD$ and $abcd$. If the number of heterozygotic pairs is n , the number of different types of germ cells is 2^n .

These 16 different types of germ cells unite, each with all the others in equal proportions. If we should represent the results of these unions, we should have for the constitution of generation F_2 a square table like that of table 2, Chapter 5, but showing 256 combinations instead of 16. But, as in table 2, there would be certain duplicates among the combinations; the total number of diverse combinations would be found to be in this case 81, or 3^4 . In general, for any number n of heterozygotic gene pairs in F_1 , the number of different gene combinations in the zygotes that form F_2 is 3^n .

(The derivation of this value 3^n may be seen as follows. If a single pair, as Aa , is heterozygotic in F_1 , this yields in F_2 the three different combinations AA , Aa and aa , (table 1,

page 117). If a second pair Bb is heterozygotic, this also yields three combinations BB, Bb and bb, and since any combination from the first pair may unite with any combination from the second, the total number of diverse combinations is 3^2 , or 9. Every pair added multiplies the result by 3, so that for n pairs the number of different combinations is 3^n .

Thus, even though we begin with but two differing stocks, in their descendants there may be produced a great number of different stocks, with diverse combinations of genes and of characteristics.

Relation to inequalities among the genes.—The relations just set forth acquire special biological significance in consequence of the fact that many of the variations among the genes are of importance for the vigour and survival of the individuals that carry them. Many of the gene modifications, as we have before seen, are in the nature of defects. This is more particularly the case with recessive genes. Often it is true that of the genes of a particular pair the dominant represents the normal condition, while the various recessive conditions are different grades of imperfection, so that the individuals that manifest the recessive condition are at a disadvantage. In other cases, much less frequent, the dominant condition represents a defect.

In view of the usual association of weakness or defectiveness with recessiveness, it is clear that there is an advantage to the organism in the doubleness of its genes. A gene derived from one of the parents may be defective; if this were the only gene of that kind present, the individual carrying it would be defective. Some of its required functions would be ill performed. But the corresponding gene from the other parent may be normal. Then, as a rule, this normal gene is dominant; it performs the required function properly, so that the individual is normal. In consequence, defective individuals are much less numerous than would be the case if their genes came from a single parent only. The doubleness of the genes acts as an insurance, preventing the harmful results of many defective genes.

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Examine now the relation of the characteristics of parents to those of offspring, particularly as to relative fitness and defectiveness, in some of the more significant results of the recombinations that occur. We deal with simpler cases first.

A. One parent defective, owing to the presence of two defective genes (aa) in one of his gene pairs. The other parent normal, having the two normal dominant genes (AA) in that pair.

All the offspring (Aa) are normal, having the characteristic of one parent to the exclusion of that of the other.

B. Both the parents are normal, but each has a defective gene in the same pair (so that they are Aa). Then some of the offspring (aa) resemble neither parent, but are defective. Other offspring (AA and Aa) are normal, like the two parents.

C. One parent defective (aa), the other normal, but bearing one of the defective genes (so that he is Aa). Then half of the offspring (aa) are like the defective parent, the other half (Aa) like the normal parent.

D. Both parents defective, each having two defective recessive genes in a certain pair (so that both are aa). Offspring (aa) are like the two parents, defective.

E. Both parents defective, but owing to two recessive genes in different pairs (Fig. 47, page 211). Offspring unlike both parents: normal, not defective.

In such cases defective parents produce normal offspring, because each parent carries a normal gene to correspond with the recessive gene of the other parent. The two parents may in such a case be defective for the same characteristic. For we know that every characteristic is affected by many genes, and can be made defective by modification of many different pairs of genes. Thus, one of the parents may be defective in the pair AA , the other in the pair BB ; the former parent is to be represented as $aaBB$, the latter as $AAbb$. The offspring are therefore $AaBb$, normal and dominant for both the pairs.

F. The two parents supplement one another in several or many pairs of genes.—Both parents may be recessive, and therefore defective or weak in respect to a number of different

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pairs of genes, but these may be different pairs in the two parents (Fig. 60, P and M). In such cases the offspring have a normal dominant gene for each of the pairs (Fig. 60, F) and will therefore show none of the numerous defects observed in the two parents. The offspring are much more vigorous than the parents, and superior to them in many ways.

This situation commonly occurs when two stocks, not too diverse, are crossed. The two stocks have lived apart for many

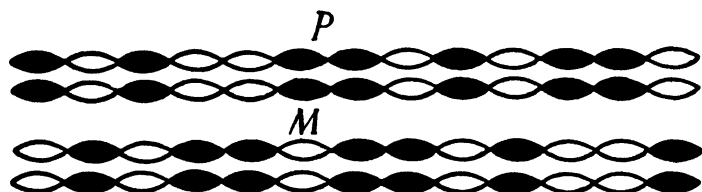


FIG. 60.—Diagram to illustrate how parents (P and M) showing many recessive defective characteristics may produce offspring with none. The spindle-shaped bodies represent genes; those represented in white are recessive, producing defective characteristics. The offspring (F) have a normal dominant gene in every pair, and are therefore without any of the parental defects.

generations. In each there has in the course of time collected through genetic variation of some sort a considerable number of recessive genes, causing weakness and defectiveness. But since in the two stocks these have been acquired independently, the recessive genes will in most cases be present in different pairs in the two stocks. Thus the genes of the two stocks show the condition indicated in the diagram of Fig. 60; each has numerous recessive gene pairs, so that each has a number of weaknesses and defects. When such stocks are crossed, the genes from the different sources supplement each other, each stock contributing a vigorous dominant gene for each pair that is weak and recessive in the other. In consequence the offspring (F₁) are far superior to the parents.

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This great improvement in F_1 when two different stocks or varieties are crossed is common in domestic animals and plants; it is commonly spoken of as hybrid vigour, or heterosis. Two varieties of maize when crossed commonly produce offspring that are stronger and more vigorous than the parent varieties, and give a higher yield of grain. The two original varieties may both be short, spindling, weak, with almost no yield of grain; their offspring are tall and vigorous with a high yield. Such 'hybrid vigour' occurs in many cultivated plants, and likewise in domesticated animals. But it is not limited to organisms under cultivation. It occurs in many cases in the classic animal for study of heredity, the fruit-fly. Two individuals with short imperfect wings or none, so that they cannot fly, the defect, however, due to different gene pairs in each case, give when mated together offspring with strong perfect functional wings. This type of relation is shown in many characteristics of *Drosophila*. It is bound to occur in any organism in which there exist many gene modifications. This is in a high degree the case with man, so that such results play a large rôle in man.

This method of action is one of the most important that occurs in genetics. It is not something that is confined to large defects, but is at work continually in connection with all sorts of characteristics, slight or marked. Human parents who are stupid and lack industry and ambition may produce children that have none of these defects, in consequence of the contribution by the parents of supplementary genes, in the way illustrated in Fig. 60. It can hardly be doubted that this is in considerable measure the origin of individuals of marked superiority, individuals of genius. They result from an unusual combination of genes formed by the contribution of supplementary genes by the two parents. Such unusual combinations may arise from two parents that are themselves not personally superior. This accounts for the not infrequent occurrence of exceptional persons, showing characteristics that make them distinguished, in commonplace families.

G. Production of inferior individuals by recombinations.—

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Results the reverse of those just described also follow from recombination of genes. By the taking apart of superior combinations and the making of new ones in which several or many defective genes come together in the same pairs, inferior, defective individuals may be produced (Fig. 61). This is most likely to occur when closely related individuals are mated, just as the production of superior individuals is most frequent when unrelated stocks are crossed. A large number of recessive genes, defective in greater or less degree,

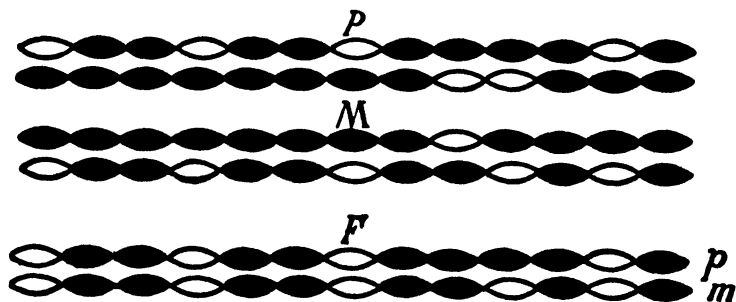


FIG. 61.—Diagram to show how parents (*P* and *M*) manifesting no personal defects may produce offspring (*F*) manifesting many defects. Each parent has a single defective gene (white) in several of his pairs, and these defective genes are in the same pairs in the two parents. In consequence some of the offspring may receive two defective genes in many pairs, as shown at *F*; these will manifest many personal defects.

are scattered through a given species, usually producing no detectable defects, because each is supplemented by a normal, dominant gene in the same pair. These defective genes are transmitted from parent to offspring, producing no effect unless two of them get together. Two individuals that have recently come from the same ancestors (hence 'related') are likely to have received from these ancestors the same defective genes in some of their pairs. When such individuals are mated, to some of their offspring each may contribute defective genes in the same pairs (Fig. 61). The result is the production of a defective individual, one that shows weak-

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nesses and abnormalities in various parts or functions. Even from two superior parents, particularly if closely related, there may be produced offspring that are inferior in one or several ways, as illustrated in Fig. 61.

In such ways are produced most of the hereditarily defective individuals. They may arise by unfortunate recombinations in normal or even superior families. They may arise also, of course, from defective parents, as set forth in paragraph *D*, above. But the numbers of the normal or intermediate families are so much greater than the numbers that are distinctly inferior or superior that the greater proportion of inferior, as well as the greater proportion of superior individuals, in such an organism as man, arise from the usual mediocre families.

Two points mentioned in the foregoing paragraphs are worthy of separate emphasis. Superior offspring are more likely to be produced through the mating of unrelated stocks, while under usual conditions defective offspring are most likely to be produced through the mating of closely related individuals. These two facts constitute the genetic basis for the undesirability of inbreeding. When extensive inbreeding occurs, many defective offspring are produced.

Yet through long-continued inbreeding, combined with selection of the best individuals for further propagation, permanently superior stocks may be produced. This matter is dealt with later (pages 293-5).

H. Production of new gene combinations through bringing together genes from diverse ancestors: The genes borne by the offspring of any two parents are of course a combination from the genes of the parents, a combination that contains half of the genes from each parent. If traced further back they are a combination of the genes borne by the four grandparents, by the eight great-grandparents and so on.

These relations are indicated in the two diagrams, Figs. 62 and 63, which give two of the possible different combinations resulting in the fourth generation (IV) from the commingling of the genes of the eight ancestors of generation I, the four of generation II and the two of generation III.

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	I	2	3	4	5	6	7	8
I	aaaa aaaa	bbbb bbbb	cccc cccc	dddd dddd	eeee eeee	ffff ffff	gggg gggg	hhhh hhhh
II	aaaa bbbb		cccc dddd		eeee ffff		gggg hhhh	
III		aaab cddd				efff gggh		
IV				aadd gffh				

FIG. 62.—See text for explanation.

In Figs. 62 and 63, the genes of each of the 8 individuals of generation I are indicated respectively by different letters (a to h), there being represented but four pairs of genes in each case. The constitution of the individual in generation IV indicates the source of his four pairs of genes; thus in Fig. 62 the individual of IV carries genes from individuals 1, 4, 6, 7 and 8 of generation I; in Fig. 63 he carries a different combination. A large number of different combinations are possible in different individuals of generation IV, even when but four pairs of genes are taken into consideration.

	I	2	3	4	5	6	7	8
I	aaaa aaaa	bbbb bbbb	cccc cccc	dddd dddd	eeee eeee	ffff ffff	gggg gggg	hhhh hhhh
II	aaaa bbbb		cccc dddd		eeee ffff		gggg hhhh	
III		aabb cccd				ceef ghhh		
IV				ccbd gehf				

FIG. 63.—See text for explanation.

In making the combination present in any individual a large proportion of the genes present in any ancestor of an earlier generation is excluded. Indeed all genes from some of

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the ancestral individuals may be excluded. So, for example, in the diagram of Fig. 62, there are in the individual of generation IV no genes of individuals 2, 3 and 5 of generation I.

The different combinations of the genes of the ancestral generations that are present in the different individuals of any given generation of course result in many different combinations of characteristics. In this way any of the genes, with the corresponding characteristics, that were scattered through many different individuals in past generations may be brought together in one individual.

A hypothetical illustration of the possibilities of this, going back only to the grandparents, may be taken from human characteristics. One of the grandparents, in consequence of his particular gene combination, may have been dull and slow, but industrious and ambitious. Another grandparent may have had natural quickness and intelligence, but also laziness and lack of ambition. Some of the grandchildren may get from one of these grandparents the genes that yield industry and ambition, from the other the genes that yield quickness and high intelligence. In this way superior individuals are formed, men that make a success of life. Other grandchildren will get the genes that yield slowness, dullness, laziness and lack of ambition all combined. These are the ne'er-do-wells, the failures. And great numbers of other recombinations may be made from the genes of the four grandparents.

The various methods of combining genes are what give origin, in any stock, whether of plant, animals or man, to exceptional individuals, both superior and inferior. From the same set of genes may be produced, by combining them in various different ways, superior individuals, mediocre individuals, and inferior individuals, all in many diverse types.

Thus it happens that in such an organism as man, or one of the domesticated animals or plants, the individuals are very different in their gene combinations, and consequently the offspring usually have combinations very different from those of their parents. They may therefore differ from their parents

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in many of their characteristics. From vigorous and efficient parents may be produced offspring that are weak and inefficient. From defective parents may be produced offspring that are normal. Superior individuals are the result of particularly fortunate combinations of genes, inferior ones the result of unfortunate combinations. In organisms living under natural conditions, on the other hand, much less variety is produced through reproduction, because the individuals that vary from the efficient types are quickly destroyed by the severe conditions under which they live.

Of the groups of organisms in which there is great diversity of genes, the constitution of a human population is typical. Such a population is made up of individuals, every one of which differs genetically from every other (save in the rare cases of identical twins). Every one is a different combination from every other. Looking at the population from the standpoint of vigour, efficiency and general fitness for life and its functions, it might be divided roughly into three groups. Forming a small percentage of all are the superior individuals, those with particularly good combinations of genes, their defective genes rendered harmless by the presence of normal ones in the same pairs. At the other extreme in the scale is the small group of the very defective, the weak and inefficient, having poor combinations of genes, their defective genes not accompanied by normal genes in the same pairs; in man the paupers and criminals and defectives. Between these two lies the large mediocre class, composing perhaps 95 per cent of the population, having a very great variety of gene combinations—not particularly excellent, nor particularly defective. A large majority of the members of the two extreme classes arise from parents of the mediocre class. When from such parents fortunate combinations are made, the genes supplementing each other, offspring are formed that pass into the superior class. In man these are the inventors, the writers, the men of science, the poets, the captains of industry. When a bad combination is made, the children fall back into the undesirable class: the vagabonds, criminals, paupers, ne'er-do-wells. A new combination is made with every child, and any

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single pair of parents can form literally thousands of diverse combinations. So from the same parents some of the children may fall in the superior group, some in the mediocre group, some in the inferior group. From the great mediocre group arise more of the superior group than from the superior group itself, and from it, too, arise more of the inferior group than from the inferior group itself. The superior group are like the cream which arises slowly from the interior of a vessel of milk. And the inferior group are the settlings, the poor genes that get together and sink to the bottom.

In all this variation resulting from the formation of new combinations of genes, it is of course true that there is in the long run and on the average a tendency for the offspring of given parents to resemble their parents more than they do other individuals, because parents and offspring have more genes in common than have unrelated individuals. For the same reason the members of a given family resemble each other more than do unrelated individuals. This is illustrated by considering the situation with respect to one pair of genes, as A and a. From dominant parents AA or Aa come a larger proportion of dominant than of recessive offspring. From recessive parents aa come only recessive offspring. Similar but less sharply defined relations hold when we consider parents differing in many genes; there is a certain degree of correlation or resemblance between individuals of the same descent. Brown-eyed parents produce a greater proportion of brown-eyed offspring than do blue-eyed parents, and vice versa. Vigorous and capable parents produce a larger proportion of vigorous and capable offspring than do parents that are weak and inefficient. Weak and inefficient parents produce a larger proportion of weak and inefficient offspring than do vigorous and capable parents. Yet it is all a statistical matter, a question of relative proportions when large numbers of individuals are taken into consideration. Usually there is great variety among the offspring of any particular type of parents, though with a tendency toward the parental characteristics.

It is to be observed that the offspring of different pairs of parents show very different degrees of similarity. The off-

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spring of parents that are alike in their genes and nearly or quite homozygous will be nearly identical in their characteristics. Thus offspring of two parents that could both be represented as AAbbCCDD would all have this same constitution and would be, except for sex differences, as similar as identical twins. In such a family identical twins could not be distinguished from fraternal twins in which the two members were of the same sex, nor indeed, except as to age, from children of the same sex born at different births.

On the other hand, offspring of parents that are heterozygous and unlike in their genes will be extremely varied. Parents whose genotype could be represented as AaBbCcDd, etc., will produce many types of offspring that may be extremely diverse. In such a family, identical or one-egg twins would differ greatly from fraternal twins.

Thus it is clear that the same degree of conventional relationship, such as that of parent and offspring, or of brothers and sisters, has very different genetic significance in different cases. If the genes of the two parents are nearly the same and nearly homozygotic, members of the same family are genetically closely alike. If the two parents differ greatly in their genes and are in a high degree heterozygotic, members of the same family are genetically very diverse, having very different combinations of genes and characteristics.

Relation of Gene Recombinations to the Transformation of Organisms in the Passage of Generations

The recombinations of genes and of characteristics that we have been considering have important consequences in transforming organisms as time passes. There are three main types of such consequences:

First, in this way there are produced combinations of genes, and therefore of characteristics, that have not before existed.

Second, in this way single qualities, powers, and dimensions may be increased beyond the degree in which they formerly existed.

Third, as a result of the recombinations of genes, charac-

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teristics may appear in the descendants that have not occurred in the ancestors.

These three types of consequences we may consider separately:

1. As we have already seen, by biparental reproduction, any quality or peculiarity of any individual or stock may become combined with any characteristics of any other individual or stock with which it can unite in parenthood. In this way may be produced combinations of characteristics that have never before been brought together. Illustrations of such changes have been given in preceding paragraphs. Such recombinations play a great rôle in relation to the fitness or adaptiveness of organisms. Thus, one stock may have strength and agility, but also poor sight and hearing. Another may have acute senses, but be weak and slow. By the mating of the two, some offspring may be produced that have all the superior qualities of the two original stocks: strength, agility, acute sight and hearing. The result may thus be individuals that are superior to any that have before existed. At the same time of course there will be produced other individuals that combine the poor qualities of the parent stocks; in the case above suggested, they will combine weakness and slowness with poor senses. Such individuals are at a great disadvantage; in time they die or fail to propagate. There may be thus left only the individuals that combine the superior qualities of the original stocks. A superior stock has been produced.

In such ways, further, the variety among organisms is greatly increased. From two stocks, each with certain combinations of characters, there are produced, by crossing, many stocks with different combinations of characters.

2. By recombinations of genes, single characteristics such as strength, vigour or development, dimensions, ability in special directions, and the like, may be increased beyond the degree in which they before existed.

We have seen in the preceding pages how such characteristics may be increased by crossing, beyond the degree in which they existed in the two parent stocks. It may thus result that they will be increased beyond the degree in

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which they have ever before existed, in the given species of organism.

This results, as we have seen, on the one hand, by the contribution of supplementary genes on the part of the two parents, as illustrated in Figs. 46, 47 (pages 210-1) and 60 (page 275). It results likewise from the recombination in the offspring of the genes that were in earlier generations separated in different ancestors, as illustrated in Figs. 62 and 63 (page 279). A concrete example is the following:

East and Hayes crossed two varieties of tobacco.¹ One of these, called Havana, averaged 20 leaves to the plant, the leaves being large, with an average area of about 7 square decimetres. The other variety, called Sumatra, averaged 26 leaves to the plant, the leaves being smaller in size, with an average surface of about 3 square decimetres. The first generation offspring (F₁) from this cross were intermediate in number and size of leaves between the two parent stocks. When the F₁ individuals were interbred, an F₂ generation was produced which showed great variation in the number and size of the leaves. Some had a mean number of leaves (26) about the same as in the variety Sumatra, with the large leaf size of the variety Havana. These plants were interbred for several generations, selecting in each case for further propagation the individuals with the largest and most numerous leaves. After several years a stock was thus produced that was superior both in leaf number and leaf size to both the original parents. It averaged about 30 leaves to the plant, and these leaves were as large as, or larger than, those of the larger variety Havana.

Thus, by crossing two stocks, a new stock is produced, showing a distinct advance on the original stocks, a stock with more numerous and larger leaves than before occurred. How was this result produced?

Without doubt it was due to the gradual collecting together into a single individual of genes that were before separated in the two original stocks. Assume (as suggested by East and Hayes) that each stock contained certain genes that tended to increase the number of leaves. Represent these

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genes by capital letters, while genes that do not tend to cause increased number of leaves are designated by lower-case letters. Then the genes of the variety Havana could be represented by some such combination as AAbbccdd, etc., while the variety Sumatra could be represented as aaBBCCDD, etc. By crossing the two and selecting the best combinations for further breeding, there is finally obtained a combination AABBCDD, etc. This contains more of the genes that tend to give increased number of leaves than either of the parent stocks; therefore it carries more leaves than either of the parent stocks.

In analogous ways, by crossing diverse races and selecting among their descendants, it is possible to obtain stocks that exceed the originals in dimensions, numbers of parts, depth of colour, vigour, power of resistance, and the like. There is little doubt that the same method of procedure gives similar results with relation to capabilities, temperament, mental characteristics of various kinds, in man. Thus by selective mating it is entirely possible that human stocks could be produced that would be superior in respect to such characteristics to any now existing.

3. By recombinations of genes, there may be produced in some of the descendants characteristics that had not before occurred.

What this signifies will best be brought out by a concrete case, a case described by Bateson.² Two varieties of primroses were crossed, one having red flowers, the other white flowers. Among the descendants in later generations there appeared flowers of many different colours: white, slightly tinged, pink, magenta, various shades of red. Some of the descendants had flowers blotched in the centre, a condition not found in the parents. In place of two colours there were a dozen or more present in diverse stocks. Also, some of the descendants differed in the form of the flower parts and in their size from the condition in either original parent. A large number of diverse colour and shape characteristics have been brought into existence.

Similar relations are illustrated in the extensive work of

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Baur in crossing two varieties of *Antirrhinum*,³ the snap-dragon. The two parent stocks differed in size, shape and colour of the flowers: one had yellowish white flowers, the other deep red. Their progeny in F₁ were as usual uniform (deep red, intermediate in size and form between the parents). In F₂ and later generations there were at least 24 different combinations of diverse sizes, forms and colours. From the two original stocks, 24 genetically diverse stocks had been formed by crossing.

The same kind of consequences follow upon crossing diverse stocks in animals. As an example, the somewhat complex case of different varieties of rabbits may be taken. In domesticated rabbits there are large numbers of varieties differing in their coat colours, as well as in other features. As to the probable origin of these many varieties we may summarize the account of Nachtsheim.⁴

In the wild rabbit it is known that many pairs of genes interact to produce the brownish grey colour of the hairy coat. This coat colour includes four or more colours—black, brown, yellow, bluish—disposed in zones on the individual hairs; together they give the general brownish-grey effect. It is known that five pairs of genes play important rôles in producing these colours; these five are designated by five letters of the alphabet. In the wild rabbit all these genes are in the dominant condition, so that for them the capital letters are employed. Thus, so far as these five pairs of genes are concerned, the wild rabbit has the genetic constitution AABCCDDGG. (Other genes affect the coat colour; for present purposes these may be left out of account.)

Nachtsheim shows that somewhat more than a century ago there were five varieties differing in colour from the wild type. Each one differed by a change in the genes of one of the five pairs. When the genes AA are changed to the recessive condition aa, no colour is produced, so that this yields a white (that is, colourless) variety. When BB is changed to recessive bb, there is no dark pigment produced, giving animals of a 'yellow-silver' colour. When GG is changed to gg, the colour is no longer distributed in zones on the hairs, but covers them

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completely. In such a case the black pigment hides all the others, so that the coat colour is solid black. Other changes are made by altering the genes C or D. There were thus five varieties differing in colour from the wild type. The different varieties had the following constitution, so far as these five pairs of genes are concerned.

The wild type (brownish-grey) is:

ABCDG
ABCDG

The five varieties each due to modification of one wild-type gene pair are:

1. aBCDG — White
aBCDG
2. AbCDG — Yellow-silver
AbCDG
3. ABcDG — Brown
ABcDG
4. ABCdG — Bluish; 'dilute'
ABCdG
5. ABCDg — Black; no pattern on the hairs
ABCDg

When any two of these five varieties are crossed, they produce in F₁ the wild type, since each contains a dominant gene corresponding to the recessive gene of the other. Thus by crossing number 3 with number 5 we obtain

ABcDG
ABCDg

And since this contains a dominant gene in every pair, these show the brownish-grey, wild-type colour. But when these F₁ individuals are mated together, we are dealing with individuals that are heterozygotic for two pairs of genes Cc and Gg. Such individuals, as we saw on page 120, produce offspring having nine different gene combinations. One of these, for example, is the variety

ABcDg
ABcDg

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This is brown, in consequence of the presence of cc; also there is no pattern on the hairs, in consequence of the presence of gg. Such solid brown animals are characterized as chocolate in colour; they constitute a new variety.

In this way, by diverse crosses among the original five colour varieties, many diverse colour varieties were formed. Nachtsheim enumerates a considerable number of these, showing the different gene combinations that they possess: lilac, madagascar (mottled yellow), light lilac, orange, sandy, and so on. By crossing among the original five colour types, a large number of additional colour types have been formed.

New colours, new shapes and the like, appearing among the descendants of a cross, are of course the result of interaction among the products of the genes brought together in the new combinations.

Thus, in sum, through the recombinations of genes in biparental reproduction, great numbers of new types are produced. Some of these show new combinations of characteristics that before existed separately. Others show characteristics increased in intensity, size, etc., beyond what previously existed. Still others show new characteristics, not before manifested. By biparental reproduction the variety among organisms is enormously increased.

Lack of permanence of the types formed by recombination of genes.—So long as ordinary biparental reproduction occurs in every generation, the characteristics produced in the way just described are not permanent beyond the generation in which they are brought into existence. For in the next generation a new combination of genes is formed. The set of genes is taken apart and recombined in new ways, giving a new set of characteristics. The very process that produced the new characteristics does away with them again. If by crossing two weak races carrying many recessive gene pairs, a large and strong F₁ generation is produced, in the way above described, in the F₂ generation the combination is broken; weak races are again produced. If, by crossing of plants having flowers of diverse colours, flowers of new colours are produced, in later

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generations these new colours may disappear, since the combination of genes that produced them is taken apart. In general, while biparental reproduction may produce good combinations from poor ones, it likewise produces poor combinations from good ones. In the succeeding generation the combinations of genes and characteristics are different from those of the earlier generation.

But in some organisms there are methods by which the new combinations made in biparental reproduction may be perpetuated, and may be multiplied, so that they become characteristic of an entire race.

The most important method by which this is accomplished is through reproduction from a single parent: fission, reproduction by budding, by bulbs, offsets, runners, cuttings; in general by what is called vegetative reproduction. In such reproduction the genes are not recombined. At the basis of such reproduction is ordinary cell division, in which each gene divides, so that all the offspring produced have the same set of genes.

In many organisms biparental reproduction and vegetative reproduction alternate. By biparental reproduction a great number of new combinations of genes are produced, represented by different individuals. Then follows a period of vegetative reproduction, in which each of the different combinations is multiplied. In this way from each combination there is produced a large number of individuals, a stock or race, all members of which have the same genetic constitution. Such a race may continue to multiply unchanged for many generations or indefinitely.

This occurs in Protozoa, in which conjugation gives the new combinations, while fission multiplies them. It occurs in Hydra, through budding after biparental reproduction, and in many other lower animals: the coelenterates, worms, ascidians. In certain other groups, as the molluscs, arthropods and vertebrates it is less common; in the higher vertebrates it hardly occurs save in the rare production of identical twins. In these groups reproduction occurs mainly by the union of germ cells, giving in each generation new combinations of

LACK OF PERMANENCE OF THE TYPES

genes, In plants vegetative reproduction occurs on a grand scale, multiplying the combinations produced in biparental reproduction.

In many organisms there is another type of uniparental reproduction, known as parthenogenesis. The female produces ova which develop without fertilization, so that there is no combination of genes from two parents. In some cases of parthenogenesis, a reduction in the number of chromosomes (and genes) occurs in forming the ova, so that the offspring produced are haploid. Haploid individuals so produced may differ in their genetic constitution from the diploid parent. Thus, a diploid parent with genes AaBb, etc., could by parthenogenesis produce haploid offspring of the different types AB, Ab, aB, ab, and so on. But when parthenogenesis continues after the haploid condition is reached, there is no further change in the gene combinations. In some other cases of parthenogenesis, the diploid condition is restored by reunion of one of the polar bodies with the ovum. This may give rise to gene recombinations for a generation or two. But as parthenogenesis continues for generation after generation, changes in the gene combinations cease. In such organisms as Rotifera and the lower Crustacea there is usually a short period of sexual or biparental reproduction, in which new combinations of genes are produced, then a period of multiplication by parthenogenesis, in which the different combinations are multiplied and subjected to the test of the conditions under which they must exist.

In all these methods of producing stocks of diverse genetic constitutions, later multiplying them by vegetative reproduction, it turns out of course that the different stocks show diverse characteristics. Some are vigorous, some are weak. Some are fitted out with full sets of efficient organs, others are defective in certain ways. Some show high resistance to unfavourable conditions, others lack resistance. Some react in an effective manner to the conditions that they meet, others do not. Some multiply vigorously and rapidly, others weakly and slowly. All these characteristics depend on the gene combinations that are present, and vary as the combinations vary.

GENERAL RELATIONS IN THE OPERATION

In general terms, some of the gene combinations are better fitted to existence under the conditions than are others.

The definitely weak and defective combinations quickly disappear, while those that are vigorous and fitted to the conditions survive and multiply. In time the population consists only of the stocks with superior combinations. At some later time, or under certain conditions, a new period of biparental reproduction occurs, the new combinations being made exclusively from the superior stocks that have survived through the period of vegetative reproduction. This process is continued for cycle after cycle. It seemingly must have a tendency gradually to improve the constitution of the existing stocks.

Relation to domestication.—Under natural conditions, which are severe and not tempered to the weak combinations, most of the new combinations produced die out, particularly the extreme and aberrant types, which are commonly not efficient. Only the best types continue to exist, and these, as it turns out, are of a somewhat uniform pattern.

But under domestication, or in the laboratory, conditions can be fitted to the new types, even if they are inefficient, even if they are weak or defective; they can be coddled and their needs supplied. Thus many types survive and multiply that in a state of nature would quickly disappear. In cultivated plants, for example, combinations that give individuals that are unusual in size, shapes and colour, are of special interest to the cultivator. They are therefore cultivated with care in greenhouses or nurseries by the use of special fertilizers and other favourable conditions. They are induced to multiply, while the common types, which in themselves may be best fitted for life, are rejected and destroyed. The situation found in nature is thus reversed: the extraordinary types are induced to multiply, the ordinary ones excluded. It thus happens that in cultivated plants great numbers of strange, striking and extreme varieties are produced, such as do not occur in the same species in a state of nature. The results appear in the extraordinary forms, sizes, colours, seen in an exhibition of dahlias, chrysanthemums, begonias, or the like.

In such plants usually the original varieties found in nature

RELATION TO DOMESTICATION

are not very diverse or showy; the number of types of form and colour are few. These are crossed; thousands of seedlings are produced. Most of these give plants not very different from the parents. These are discarded. Others, with unusual combinations of genes, give the large, showy individuals of colours and shapes diverse from those of the original varieties. These are induced to multiply, by bulbs, cuttings or other vegetative methods, until from the single plant an entire variety is produced.

If individuals of these striking varieties are allowed to cross and produce seeds, it is well known that they do not 'breed true'. The unusual combination of genes that produced them is broken up by the processes of biparental reproduction. New combinations of genes are produced, and most of these give origin to commonplace plants like the original varieties from which the showy types were produced.

Organisms in which uniparental reproduction does not occur.—There are many organisms in which it is not possible by vegetative reproduction to perpetuate and multiply the new combinations produced in biparental reproduction, for vegetative reproduction does not occur. This is notably the case in higher animals and man, as also in some lower animals, and in some plants. In most such organisms there occur sporadic cases of the production of identical twins or the like, which illustrate in principle the multiplication of given gene combinations by vegetative reproduction. But such processes are not continued for successive generations, so that they cannot give origin to vegetative races.

In such organisms there is a slow, difficult and imperfect method of perpetuating some of the new combinations of genes and of characteristics that result from biparental reproduction. This is by inbreeding: the mating of individuals that have come from common ancestors, the mating of 'close relatives'. Inbreeding is an unsatisfactory and uncertain method compared with vegetative reproduction, but if carried on for many generations it may yield permanent stocks having new character combinations.

GENERAL RELATIONS IN THE OPERATION

The principles on which inbreeding acts are the following:

1. By inbreeding for successive generations homozygous stocks are produced.

2. Homozygous stocks breed true; that is, when they reproduce sexually they do not produce new gene combinations. The offspring have the same gene combinations as the parents.

3. Thus, if in this way a homozygous stock is produced having the new combination of characteristics that it is desired to preserve, this stock is permanent (so long as it does not again interbreed with other stocks).

The mechanism of the operation of inbreeding may be illustrated from simple cases. Suppose that a stock is heterozygotic for a single pair of genes, Aa , and that it is desired to obtain a permanent stock with the characteristic represented by the dominant gene A . If we breed together two members of this stock, we obtain the three combinations AA , Aa , and aa . The two former have the character A which we wish to preserve. If we breed together such individuals as have this character, we obtain in different cases the pairs $AA \times AA$, $AA \times Aa$ and $Aa \times Aa$. The first of these, $AA \times AA$, will yield offspring AA , with no admixture of other types. Continuing to breed together $AA \times AA$, we obtain a stock in which all the individuals have the character A .

Or, similarly, if we wish to obtain a stock all of which have the recessive character represented by a , we have but to breed together the recessive individuals $aa \times aa$; the descendants are all aa .

If the original parents are heterozygotic for two pairs, so that they may be represented as $AaBb$, when they interbreed we obtain the nine different gene combinations given on page 120. Some of these show the characters represented by the two dominant genes AB , some show one dominant and one recessive, Ab or aB , some show two recessives, ab . Suppose that we wish to obtain a permanent stock with characters Ab . We interbreed all the individuals showing those characters. Some of them will not breed true; such for example are $Aabb \times AAbb$; these will yield some recessives, $abab$. But if

PRINCIPLES OF INBREEDING

in some of our matings we breed together the homozygotes $AAbb \times AAbb$, these give only offspring $AAbb$. These when bred further remain constant.

When the number of gene pairs in which the parents are heterozygous is greater, the process of producing permanent homozygous races having certain characteristics is slower and more uncertain. It may require many generations of selective inbreeding before a permanent stock is established.

It is in this way that have been produced the various 'pure' or constant races or breeds of dogs, rabbits, fowls, and cattle. In many such races there still remain a few gene pairs that are heterozygotic. Thus, in a race in which most individuals are $AABBCcDD$, etc., there might be a few individuals $AABBCcDD$. The recessive gene c will have no effect, until it happens that two such individuals mate, whereupon some of the offspring have the constitution $AABBccDD$. The recessive character due to cc will then unexpectedly appear, giving individuals that fail to show some of the usual characteristics of the breed. Such individuals are not allowed to breed further.

Thus it is clear that by the production of new gene combinations in biparental reproduction, and by making these lasting through vegetative reproduction or by inbreeding, many new types or breeds, perhaps differing greatly from the original parents, are produced. This is a very large factor in bringing about the great variety observed in organisms.

NOTES AND REFERENCES ON CHAPTER 12

1. Page 285. E. M. East and H. K. Hayes (1914), 'A Genetic Analysis of the Changes Produced by Selection in Experiments with Tobacco', *Amer. Naturalist*, vol. 48, pp. 5-48.

2. Page 286. Wm. Bateson (1909), *Mendel's Principles of Heredity*, Plate VI, p. 294.

3. Page 287. E. Baur (1924), 'Untersuchungen über das Wesen, die Entstehung und die Vererbung von Rassenunterschieden bei *Antirrhinum majus*', *Bibliotheca Genetica*, Bd. 4, 170 pages, 5 plates.

4. Page 287. H. Nachtsheim (1922), 'Die Entstehung der Kaninchenrassen im Lichte ihrer Genetik', *Zeitschrift für Tierzüchtung und Züchtungsbiologie*, Bd. 14, pp. 53-109.

13

GENETIC VARIATIONS

Changes in the Structure and Operation of the Genetic System

The intensive studies of the genetic system and its operation that have been made in the last thirty-five years have shown that this system may become changed as time passes and that these changes give rise to alterations in the inherited characteristics of organisms. Such changes may be called genetic variations. Genetic variations of a number of different types are known, and there may be other types as yet unknown. The known types represent changes in the structure and operation of the genetic system—of the chromosomes and genes.

The genetic system presents three diverse aspects, each of which may become altered, so that each of the three yields a distinctive type of genetic variation. The genetic system, as we have seen, is composed of many diverse organic materials, the genes, arranged in definite structures, the chromosomes, which together form a complex apparatus. In different individuals this apparatus has different combinations of genes.

1. Changing the combination of genes that are present in the system gives one type of genetic variation. This occurs in the normal processes of biparental reproduction and Mendelian inheritance. We have already given an account of this, and of its consequences, in Chapter 12. We there saw that it may give rise to new combinations of characteristics, to characteristics increased or decreased in dimensions or intensity beyond what before existed, and to new characteristics. It is

the commonest and one of the most important kinds of genetic variation.

2. A second method of producing genetic variation is by changes in the structure of the genetic system.¹ The numbers of chromosomes present may be altered. The chromosomes may become broken into pieces, or united together in various ways. Genes may be lost. The arrangement of the genes in the chromosomes may be changed. Genes may be transferred from one chromosome to another. All such changes cause alterations in the inherited characteristics, or in the method by which the characteristics are inherited.

3. A third type of genetic variation arises from changes in the physiological action of single genes, resulting either from a chemical change in the constitution of the gene, or from other causes. Such changes in the action of single genes are commonly called gene mutations.

Genetic variations resulting from gene recombinations have been dealt with in Chapter 12. Here we take up the other two types of genetic variation.

Genetic Variations resulting from Changes in the Structure and Operation of the Genetic System

The genetic system, as we have seen, is a mechanism operating in a complicated fashion. Like other mechanisms, it is subject to getting out of order: to accidents, breaks, and irregularities. Such accidents and irregularities may make impossible the operation of the genetic system, and so cause death, or sterility. But in many cases the system continues operating, but in a changed manner, and this gives rise to changes in the characteristics that depend on the system. Changes so produced are now under investigation by many students of genetics, and the results are of much importance for the understanding of inheritance and variation. There are two main classes of such genetic variations. One consists of changes in the number and grouping of the chromosomes, the other of breakage and reunion of the parts of the chromosomes. We consider these separately.

1. Changes in the Number and Grouping of the Chromosomes

The commonest type of irregularity in the action of the genetic system and that of which the consequences are best known is that known as non-disjunction. This has been described on earlier pages (page 69 and Fig. 20). In rare cases, in forming germ cells, the two members of a pair of chromosomes fail to separate. In consequence one germ cell is formed which has two members of this pair, while the other has no member of this pair. This gives rise to many further irregularities in the individuals formed by these germ cells.

When the germ cell with two chromosomes of a pair (Fig. 64, A) unites with one of the usual germ cells having a single chromosome of that pair (B), a zygote is formed that has three chromosomes for this pair instead of the usual two (Fig. 64, C). Such zygotes are called trisomics. The individuals developed from such trisomic zygotes have the genes of this chromosome in threes instead of in pairs.

Also when the germ cell having no chromosome of a certain pair (Fig. 64, D) unites with a typical germ cell, a zygote and individual is formed with only one chromosome of that pair, the genes single instead of in pairs (Fig. 64, F).

Many cases in which such changes have occurred have been found in many different animals and plants. Such changes in the numbers of chromosomes alter the development, and so yield individuals having different characteristics from those which have all the chromosomes in pairs. The differences result mainly from differences in the balance among the genes and chromosomes (compare page 75). A trisomic individual differs in certain respects from the typical individuals; an individual with but one chromosome in place of two differs in another way. These matters have been most thoroughly studied in certain plants, particularly in *Oenothera*, the evening primrose, and in *Datura stramonium*, the Jimson Weed.²

Just what changes are made in the inherited character-

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istics depends on which of the several pairs of chromosomes it is that has had a chromosome added or subtracted. The different chromosome pairs of course are diverse as to their genes and have diverse effects on characteristics. Hence,

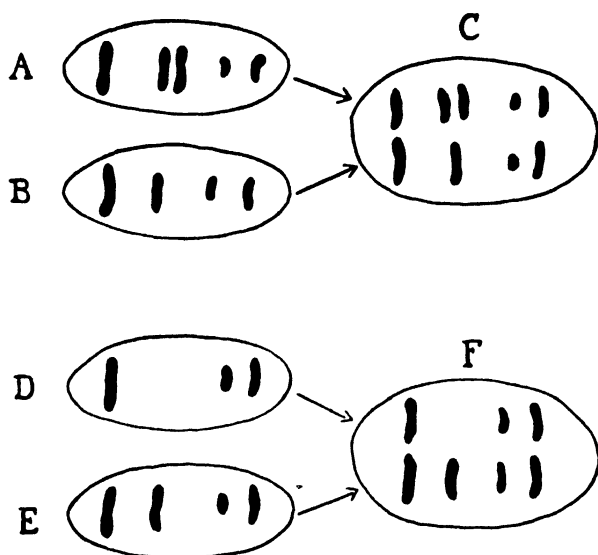


FIG. 64.—Diagram to illustrate the formation of trisomics (C) and zygotes with but one chromosome in one of the pairs (F). The basic number of chromosome pairs is here four. At A, a germ cell with two chromosomes of the second pair (from the left) unites with a normal germ cell B to form the trisomic C, which has three chromosomes for the second pair. At D, a germ cell lacking a chromosome of the second pair unites with a normal germ cell E to form the zygote F, having but one chromosome of the second pair.

adding a chromosome to one pair, or subtracting a chromosome from that pair, has very different effects from the same change in another pair. Since any organism has several or many pairs of chromosomes, a large number of different genetic types can be produced in such ways.

In *Datura*, for example, there are twelve pairs of chromosomes. Adding a third chromosome to any one of the pairs

GENETIC VARIATIONS

gives in each case individuals of different characteristics. Hence twelve different types are producible through adding a chromosome in different cases to each of the twelve different pairs. Also, twelve other varieties are formed by taking away, in different cases, one chromosome from each of the twelve pairs. Many or all of these twenty-four types have been produced and studied by Blakeslee and his associates. The different types differ markedly in the form and size of the fruits, leaves or flowers, or in the general habit of the plant.

In other cases two of the chromosome pairs are found each to have a third chromosome added to them. Such individuals are known as double trisomics. For 12 chromosomes there are 66 different combinations in which one chromosome can be added to each of two pairs. This yields 66 additional types, many of which have been identified. And there are 66 other types producible by subtracting one chromosome from each of two pairs, in the 66 possible combinations of 2 from 12.

When individuals having three chromosomes in place of one of its pairs form germ cells, some of these germ cells contain two chromosomes of that pair, others but one (Fig. 65). When a zygote is formed by union of two germ cells, each of which contains two chromosomes of the given pair, there is produced an individual that has four chromosomes to one of its pairs (Fig. 65, G); its genes are thus in fours, so far as this chromosome is concerned. Such individuals are known as tetrasomics. They have different characteristics from any of those spoken of above.

There are in *Datura* twelve different varieties that can be formed by giving four chromosomes in place of two, in different cases, to each of the twelve chromosome pairs. And 66 additional types can be formed by giving four chromosomes to each of two of the pairs, in the 66 different combinations in which two can be selected from twelve.

The number of possible diverse types thus becomes large; in *Datura* with its twelve pairs of chromosomes we have already enumerated 234 possible diverse types. It might appear that varieties could be multiplied practically indefinitely in this way by adding or subtracting one or two to each of three

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pairs of chromosomes, then to each of four, and so on. But it turns out that if more than two pairs are thus changed by addition or subtraction (yet not all the twelve are so changed) the individual cannot live. It appears to be too unbalanced for development to occur.

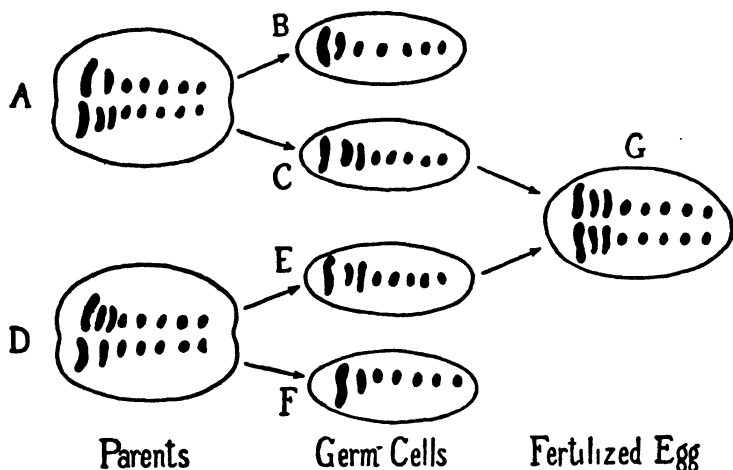


FIG. 65.—Diagram of the formation of a tetrasomic (G) as a result of germ cell formation by trisomics (A and D). The basic number of chromosome pairs is here seven. The two trisomics A and D each have three chromosomes for the second pair from the left. In forming germ cells, two chromosomes of this pair pass into one set of germ cells (C and E), only one into the other set (B and F). By union of C and E, a zygote G is formed having four chromosomes in place of two, for the second pair; this is a tetrasomic.

Yet if all the twelve chromosome pairs lack one chromosome, or if all have one or two additional chromosomes, the individuals survive and develop. There is in such cases no lack of balance; all pairs are decreased or increased equally. In *Datura* there are known types that have but twelve chromosomes, one in place of each pair. These are of course haploids; they live and develop. Other types are known in which there are three chromosomes in place of each pair, so that 36 chromosomes are present. These are called triploids. Still

other *Daturas* are known in which there are four chromosomes for each of the twelve pairs, making 48 in all; these are tetraploids. In all these cases, the types differ from the usual diploid individuals, having but two chromosomes for each of the 12 pairs, or 24 in all.

Further, by adding or subtracting one or two chromosomes to the different groups ('pairs') in the tetraploids or other types, a great number of varieties are producible from a single original diploid type. Fig. 66 gives diagrams of a number of those diverse types. Blakeslee and his associates have produced in *Datura* and studied 89 different types of *Datura* produced in such ways. And these are only a fraction of those that are possible. Computations show that in *Datura* there must be 3,620 different possible types or varieties producible from the typical diploid, by altering the grouping of the chromosomes in the ways set forth above. There is reason to believe that all of these can be produced and that they will live.

The conditions in *Datura* are not exceptional. They are found in many organisms, particularly in plants. They have been extensively studied in various species of *Oenothera*, the evening primrose. In this plant, as in *Datura*, there are many different types or varieties, resulting from changes in the grouping of the chromosomes and genes.

It was in one of the species of the evening primrose, namely, *Oenothera lamarckiana*, that Hugo de Vries made his famous investigations which were published in the year 1901 in his two-volume work known as *The Mutations Theory*, a work which may be said to constitute the beginning of modern genetics. Most, though not all, of the changes in inherited characteristics which de Vries described, and which he called mutations, were the result of changes in the grouping and numbers of the chromosomes and genes, of the sort described above, although this fact was not discovered till much later.

Non-disjunction and the phenomena resulting from it occur in animals as well as in plants. In Chapter 4 an account was given of some of the phenomena of this character in

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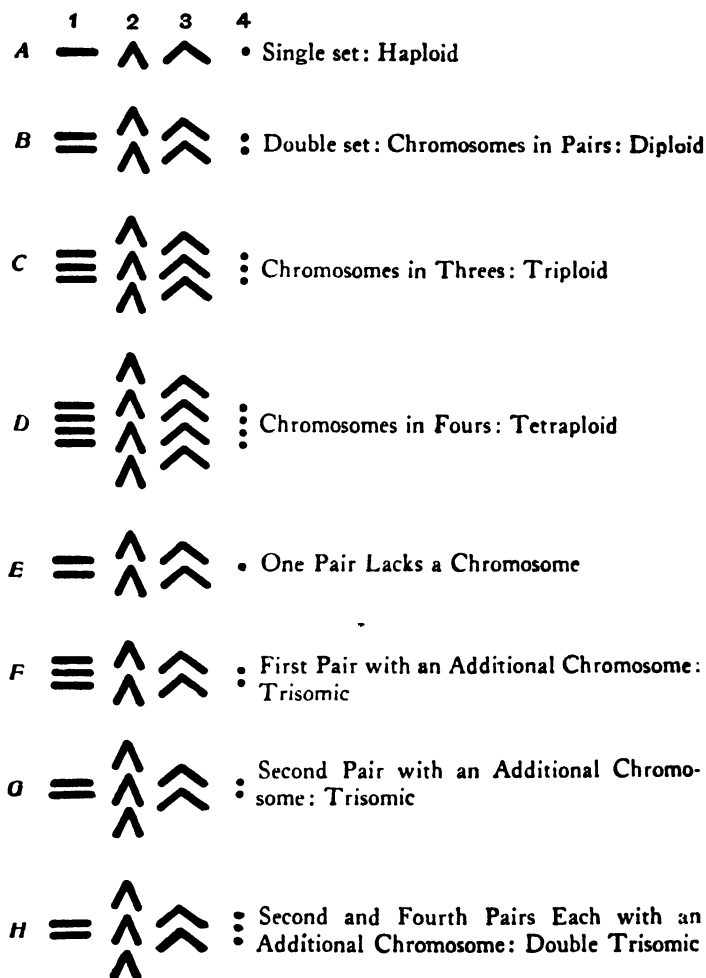


FIG. 66.—Diagrams to show some of the different groups of chromosomes that produce diverse types of organisms. The basic number of chromosomes is taken as four. A, chromosomes not in pairs, the haploid condition, found in germ cells and in some organisms. B, chromosomes in pairs, the diploid condition found in most organisms. C to F show other conditions known to occur.

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Drosophila. On the whole, production of diverse varieties in this manner seems to be less common in animals than in plants.

Most of the varieties thus produced by altering the number and grouping of the chromosomes are not permanent in biparental reproduction; that is, the peculiar characteristics of the parents are not fully reproduced in the descendants. This is because the irregularities in the chromosome numbers cause irregularities in germ cell formation and fertilization, with the result that the offspring have different chromosome groupings from those found in the parents, and therefore show different characteristics. In varieties having odd numbers of chromosomes to the 'pair', as in triploids and trisomics, the different offspring are bound to receive different chromosome combinations, and therefore to be of diverse types. Among the offspring are usually some individuals in which the chromosome grouping is so irregular and unbalanced that they cannot live. It is only the cases in which all the chromosome pairs are doubled—that is, the tetraploids—that are inclined to reproduce themselves normally, thus forming a lasting variety. Tetraploid varieties are known in many plants. In tetraploids the cells, containing twice the usual number of chromosomes, are larger than in the common diploids. In consequence the individuals themselves are stouter and larger, forming so-called giant varieties. One of the well-known 'mutants' found by de Vries, *Oenothera gigas*, was of this type. It was large and thick-stemmed, and its cells carried 28 chromosomes in place of the diploid number 14.

The varied races produced by changes in chromosome numbers may in many plants be perpetuated through vegetative reproduction; that is, by cuttings, bulbs, runners, offsets, and the like. This method of reproduction does not disturb the chromosome arrangements. In cultivated plants that multiply vegetatively, alterations in the number and arrangement of the chromosomes seemingly play a large rôle in producing the great variety of types that are to be observed. Presumably many of the extraordinary forms, sizes and

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colours seen in an exhibition of dahlias, chrysanthemums or the like are the result of such changes. Many of these diversities, as we saw in Chapter 12, are due to the recombinations of genes resulting from crossing of different stocks. Others are the result of the chromosome changes here under consideration. Both types may be perpetuated in uniparental reproduction.

There is much evidence, further, that changes in the number and grouping of chromosomes have played a rôle in producing the different stocks, varieties, and perhaps species found in nature. As we have seen, in such ways there are produced haploid, diploid, triploid and tetraploid plants. If we call the number of chromosomes in the haploid set by the letter n , then we may say that there are producible stocks carrying either n , $2n$, $3n$ or $4n$ chromosomes.

In wild plants it is found that many closely related varieties or species have differences of just this kind. Thus, in the roses the number of chromosomes in the haploid set was apparently originally 7. Varieties of roses are found having 14 (diploids), 21 (triploids), and 28 (tetraploids). However, the numbers go even beyond this; there are varieties or species with 35, 42 and 56 chromosomes. Thus there are varieties carrying $2n$, $3n$, $4n$, $5n$, $6n$ and $8n$ chromosomes (n being 7 in each case). These varieties having several sets of chromosomes are known as polyploids.

Polyploids are common in many plants. Different varieties or species of wheat have their chromosomes in multiples of 7: some have 14 chromosomes, some 28, some 42. The chromosomes in the chrysanthemums go by sets of 9: different varieties or species have 18, 36, 54, 72 or 90 chromosomes. In different *Oenotheras* the chromosomes are in multiples of 7, in *Potentillas* of 8, and so on. Seemingly the polyploids must have been derived from original haploids or diploids by increase in the number of sets of chromosomes.

Similar conditions are found in animals. In some starfishes the chromosome numbers are based on sets of 9; there are some species with 18, others with 36 chromosomes. Some varieties of cyclops have 6 chromosomes, others 12.

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which prevailed before the break and reunion, the opposite of the order shown on such gene maps as Fig. 38. Thus, if the original order of the genes was a-b-c-d-e-f-g-h-i-j-k-l-m-n-o-p-q-r-s-t, after the break and reunion the order may be a-b-c-d-e-n-m-l-k-j-i-h-g-f-o-p-q-r-s-t, the genes between e and o being reversed in their order. This reversal in the order of the genes can be discovered by tests of breeding and linkage in later generations. A great number of cases of such inversions of the middle part of the chromosome have been studied—the order of the genes reversed in the middle part but not at the two ends. This reversal is an extraordinary phenomenon, requiring explanation.

(3) In other cases the middle piece drops out completely and is lost. The two end pieces then reunite at their broken ends. Thus a short chromosome is produced, lacking all the genes of the middle region, but still carrying those near the two ends. These are known as deletions, the middle part being deleted. A large number of such deletions are known.

A third strange result is often produced when the chromosomes are broken by radiation. If the usual two breaks are in two different chromosomes of the same cell, then frequently these two chromosomes exchange parts. The broken end of one piece from one chromosome unites with the broken end of one of the pieces from the other. The other two pieces of the two chromosomes similarly unite. Thus we get two newly combined chromosomes, each made up of two halves that formerly belonged to two separate chromosomes. Such exchanges, or translocations as they are called, are known in many cases.

With relation to these changes, there are several questions that require answers. First, how does it happen that in a cell two chromosome breaks occur instead of one? Second, how do the broken ends find each other and reunite—often resulting in a new combination? And third, how does it happen that in such reunited chromosomes the order of the genes in the middle piece is commonly reversed?

There is a simple explanation of these strange relations, one that throws light on the way the breakage is brought about.

BREAKAGE AND REUNION OF PARTS

The numerous long thread-like chromosomes in the cells undergoing radiation lie close together and are more or less curved, coiled and tangled. They may cross each other and come in contact, but under ordinary conditions when this happens they do not stick together.

But under the action of radiation, the chromosomes change physically in such a way that when they come in contact by crossing at a certain point they stick together. There are indications that the chromosomes have a transparent sheath, which keeps the essential parts of the chromosomes—the genes—within the sheath from coming in contact. By radiations this sheath is seemingly dissolved or modified in spots, so that the chromosomes within it may actually come in contact. When this occurs they stick together, and through strains set up in the intracellular processes they may break. The rest of the process will be best understood from a hypothetical example. Suppose that a chromosome in this adhesive condition becomes looped, so that its two limbs cross and come in contact (Fig. 67, A). The parts in contact stick together, and the chromosome breaks at the-point of adhesion. The chromosome is thus left in three pieces, a central loop and two end pieces (Fig. 67, B).

The three broken ends are still in contact, and there occur at the tips growth processes, so that the broken ends, some or all, may reunite. The two end pieces may reunite, leaving the loop free. In that way are produced the 'deletions', short chromosomes lacking all the middle part. In such cases the free loop degenerates or is lost.

In other cases the two end pieces may reunite with the ends of the central loop. Sometimes the union may be with the same ends as before; then there might be no evidence that any break had occurred. But in other cases, since the four ends are all close together, each end piece may unite with the other end of the loop from that with which it was before united. This produces the inversions (Fig. 67, C). The chromosome now has its two end parts as before, but in its middle part the order of the genes is reversed.

If the accidental crossing or contact is between two differ-

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ent chromosomes (Fig. 67, D), then they adhere at the point of crossing, and both may break there. Then the ends, in becoming reunited, may in some of the cases readily exchange partners. Thus are produced the translocations: two chromosomes that have exchanged parts (Fig. 67, E).

Thus all these remarkable phenomena find a simple explanation through consideration of the conditions that exist within the cells. No other explanation than one along the lines suggested seems possible. It appears clear, therefore, that the breaks and other chromosome irregularities resulting from radiation are not due to the striking of an electron against the chromosome at the point of breakage, but to the sticking together of the chromosomes. The radiation seemingly makes some general physical or physiological change in the cell contents, resulting in the ready adhesion and breaking of the chromosomes.⁵

We now come to the genetic results of these changes, the alterations in inheritance that they bring about. There are a number of different types:

When a chromosome is broken into two pieces, genes that were formerly present in a single chromosome, and were therefore linked in inheritance, have become separated into two pieces, which may be passed on separately to members of the next generation. Thus, if the two pieces are both passed on, certain genes, that in earlier generations were linked, are in later generations not linked.

Often, however, one piece of a broken chromosome is lost. This is because in cell division each chromosome has attached to it at a certain point (usually either at one end or at the middle) a single spindle fibre, which holds it in place. When a chromosome is broken, one of the pieces is without the spindle fibre attachment, so that it may get lost. In order that such a piece shall be carried through the cell divisions in the usual way, it must become attached to another piece that has a spindle fibre attachment.

When a piece of a chromosome is entirely lost, carrying with it of course a number of genes, the organism is unable to develop, unless it contains also another chromosome of that

BREAKAGE AND REUNION OF PARTS

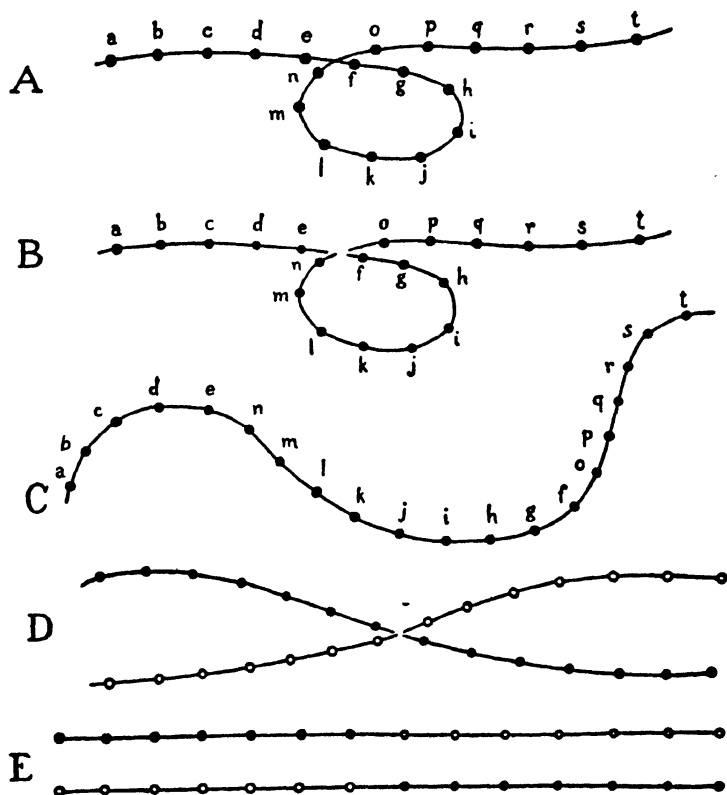


FIG. 67.—Diagrams to illustrate the method of formation of inversions, deletions and translocations. A, chromosome in the thread-like condition, looped, with its two limbs in contact where they cross. B, the chromosome broken into three pieces at the point of crossing. C, inversion; the genes f to n are reversed in their order, as a result of the union in B of the region of the gene e with that of the gene n, and of the region of gene f with that of gene o. D, two thread-like chromosomes in contact where they cross; a break occurs at this point. E, translocation, produced by the reunion in D of the halves of one chromosome with the halves of the other.

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pair in which these genes are not missing. As we saw on pages 187-8, complete deficiency for even a single gene usually prevents development.

In translocations, there is of course a change in the method of inheritance. If a piece of an autosome is thus transferred to an X-chromosome, the characteristics dependent on the genes in the transferred piece are in later generations no longer inherited in the autosomal or typical Mendelian manner, but according to the rules of sex-linked inheritance. Conversely, if a piece from X is translocated to an autosome, the inheritance of certain sex-linked characters is changed to the autosomal type. Many cases of this kind are now known. They demonstrate in a striking way the dependence of the method of inheritance on the location of the gene in a particular chromosome; when the location is changed the method of inheritance changes correspondingly.

When the order of the genes is reversed in a certain part of the chromosome, as indicated in Fig. 67, C, this of course changes the relation of genes to each other. Certain genes that were close together in the chromosome are now far apart; certain others that were far apart are now close together. This results in changes in the linkage ratios of the genes. Furthermore, if such a chromosome with part of its genes reversed in order is present in the same cell with another of the same pair in which the genes retain their usual order (Fig. 68), this prevents any exchange of genes in the parts that are not in the same order, so that there is no crossing-over of characters dependent on these genes. Inversions of parts of the chromosomes are frequently discovered through the failure of certain chromosomes of the same pair to exchange genes. Further study then as a rule shows that an inversion has occurred in one of the chromosomes.

Another effect of great interest results from breakage of chromosomes. Usually some of the genes near the points of breakage become altered in their physiological action. They no longer affect the characteristics of the organism in the way they did before the breakage occurred. The changes in gene action are of the kind that have been commonly called gene

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mutations (see next chapter), so that 'chromosome breakage causes gene mutations'. The nature of the changes in the action of particular genes resulting from chromosome breakage will best be grasped from certain examples.

Schultz and Dobzhansky⁶ have described in detail the changes in characteristics resulting from breakage of the second chromosome in *Drosophila* (see Fig. 38 for map of this second chromosome). A piece of the chromosome extending

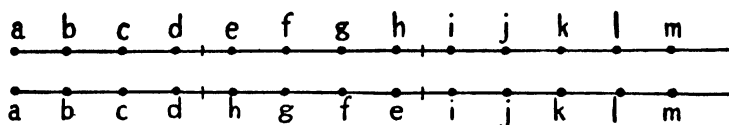


FIG. 68.—Diagram of two chromosomes at the conjugation stage, one containing an inversion (*e* to *h*), so that there is no crossing-over, or exchange of genes in that region. The genes *e* to *h* of the upper chromosome cannot conjugate normally with the genes *h* to *e* of the lower chromosome, so that no exchange occurs between those parts.

from about the locus 55 of the map to about the locus 104.5 had been broken out and replaced in the inverted position, so that all the genes between 55 and 104.5 were in the reversed order from that shown on the map of Fig. 38. At or near the two points of breakage certain of the genes had become changed in their action. At the break near the right or lower end of the chromosome, at about 104.5 three genes had become changed. One of these affects the colour of the eye. When it is in the normal or unchanged condition the eye is red. After the breakage, this gene became unstable in its action. In some of the cells it produced its usual effect, in others it did not, so that the eye showed patches of darker and lighter colour. In addition, the changed gene when in operation caused the eye colour to be darker than usual, giving a colour known as 'plum'.

The other two genes that were changed in the region of this break affected the growth of the bristles borne on the body; one is known as 'minus', the other as 'abbreviated'. Both of these genes were made unstable, so that in some of

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the body cells they operated, in others they did not, giving bristles of different sizes in different parts of the body.

At the other region of breakage, at about the locus 55, another gene was made unstable in its action. This is the gene 'light', at locus 54.5, which has an effect on the eye colour. It was found by Schultz and Dobzhansky that this gene operated normally in some of the cells, while in others it did not, thus giving under some conditions a mottled appearance to the eyes. There was also a lethal effect at this break; when both chromosomes of pair II had the break at locus 55, the individuals did not develop.

Thus by breakage of the chromosome II there were produced on genes near the points of breakage the following effects:

1. A dominant eye-colour change or mutation.
2. Instability of four different genes.
3. A change that was lethal when homozygous.

No other case has yet been so thoroughly studied as the one just described. But in a considerable number of cases breakage of a chromosome is known to make certain genes near the points of breakage unstable, so that they operate in certain cells, but not in others. Thus they produce a body that has diverse inherited characteristics in its different parts, a condition commonly spoken of as mottling.

In other cases breakage of a chromosome causes a simple change in some inherited characteristic, giving a dominant or a recessive 'mutation'. For discussion of these, see the next chapter.

What is the nature of the effect on the genes that is produced by breakage of the chromosome? On the one hand, chromosome breakage is in the nature of a laceration, an injury, to the tissues. The effects on the genes near the point of breakage may be essentially small-scale injuries, affecting single genes, induced at the same time as the greater injuries seen in breaks, deletions and deficiencies. The fact that some of the genes are put completely out of action, so that they will no longer permit development, and that others

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are made weak and unstable, seems to suggest such an interpretation.

Another possibility that is at present under examination is the following. When a chromosome breaks, the pieces usually reunite in an unusual position, so that genes near the region of the break are in closer relation to other genes than those that are normally near to them. It is suggested that possibly the effect of a gene depends on its position with relation to other genes, presumably on the interaction of genes that are close together. This is spoken of as a 'position effect'.⁷ According to this suggestion, when a gene changes its position with relation to other genes, it may change its method of action. In one position its effect is to produce what is commonly called the normal or unchanged characteristic. In another position it becomes weak and unstable in its action, or it produces a different effect on the characteristic, an effect that has been called a mutation. This matter will be discussed further in the chapter on mutations.

Changes in the arrangement of the genes within the genetic system appear to occur somewhat frequently in certain plants. In *Datura* and *Oenothera* it is found that certain stocks differ from others in the fact that chromosomes of different pairs have exchanged parts, as happens in the translocations induced by radiations. In this way have been produced a considerable number of different stocks, having the same genes, but with the genes differently combined in chromosomes in the different stocks.⁸ Usually such differences produce, in these plants, no difference in the action of the genes, a fact that appears inconsistent with any general validity of the hypothesis of a 'position effect'. The diverse races differ, of course, to a certain extent in the linkage of the genes.

It thus turns out that, in some species at least, the way the genes are arranged in the chromosomes is less stable than had been supposed. Blocks of genes have been shifted about from one chromosome to another, without causing any marked change in the action of the genes.

In another way changes in the grouping of the genes ap-

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pear to have played a part in producing diverse varieties or species. In any given variety or species, the genes are grouped into a certain definite number of chromosomes: in man 48, in the fruit-fly 8, in the horse-worm 2, and so on. This grouping of the genes of course has an effect on inheritance, since there is a linkage group for each chromosome pair. As we have seen, sometimes a chromosome is broken into two, thus adding one to the number of linkage groups. In other cases

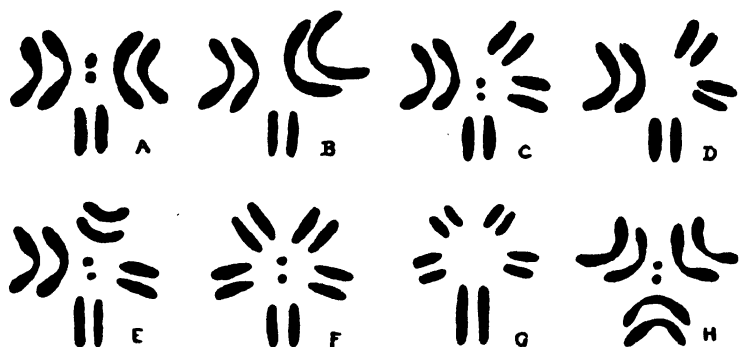


FIG. 69.—The chromosome groups (A to H) in various different species related to *Drosophila melanogaster* (A), illustrating how that of one species is producible from that of another by slight changes in the union or separation of certain chromosome parts. After Metz (1916). See text.

two chromosomes or parts of chromosomes may unite, decreasing the number of linkage groups.

When related species or varieties of animals or plants are compared, it is often found that they have groups of chromosomes so differing as to suggest that one has been derived from another in the ways just described; that is, by breaking, or by union, of certain chromosomes. This is, for example, the case in different species of *Drosophila* and of other genera related to *Drosophila*. Excellent figures showing the chromosome groups in different species have been published by Metz; some of these are copied in our Fig. 69. Type A, which occurs in the common fruit-fly, has four pairs of chromosomes, one pair straight, two pairs V-shaped, one pair small and

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nearly spherical. Type B, in another species, is like type A except that the small chromosomes have united with some of the larger ones, leaving but 3 pairs. Type C, found in a third species, is like type A except that the chromosomes of one of the V-shaped pairs have broken at the point of the V into two straight chromosomes; so there are in this type 5 pairs. In type F, both the V pairs of type A have broken into two straight chromosomes, giving six pairs instead of four. The various other types result from similar rather simple changes. There are many other cases of related species having chromosome groups that thus differ by slight alterations.

NOTES AND REFERENCES ON CHAPTER 13

1. Page 297. Genetic variations resulting from changes and irregularities in the genetic system have been very fully described and figured in C. C. Hurst's *The Mechanism of Creative Evolution* (1932), 365 pages. See also T. H. Morgan (1928), *The Theory of the Gene*, 343 pages; and (1932), *The Scientific Basis of Evolution*, 286 pages.

2. Page 298. The work on *Datura* is by A. F. Blakeslee and his associates. See A. F. Blakeslee and J. Belling (1928), 'Chromosomal Mutations in the Jimson Weed, *Datura stramonium*', *Journal of Heredity*, vol. 15, pp. 195-206; and the references there given. For details as to *Oenothera*, see R. R. Gates (1928), 'The Cytology of *Oenothera*', *Bibliographia Genetica*, vol. 4, pp. 401-492.

3. Page 306. See the lists of the chromosome numbers of different species of animals and plants in Wilson's *The Cell in Development and Heredity*, pp. 855-865.

4. Page 306. Much of the knowledge of the effects of radiation in organisms, and particularly in *Drosophila*, is due to the work of H. J. Muller and his associates. The account of the text is based largely on the following:

H. J. Muller and A. Dippel (1928), 'Chromosome Breakage by X-rays and the Production of Eggs from Genetically Male Tissue in *Drosophila*', *British Journ. of Experimental Biology*, vol. 3, pp. 85-122; H. J. Muller (1930), 'Types of Visible Variations Induced by X-rays in *Drosophila*', *Journ. of Genetics*, vol. 22, pp. 299-334; H. J. Muller and E. Altenburg (1930), 'The Frequency of Translocations Produced by X-rays in *Drosophila*', *Genetics*, vol. 15, pp. 283-311; H. J. Muller (1932), 'Further Studies on the Nature and Causes of Gene Mutations', *Proceedings of the Sixth International Congress of Genetics*, vol. 1, pp. 213-255.

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The papers above listed contain references to a large part of the extensive literature on this subject.

5. Page 310. The account given above is based mainly on the paper of Muller, 1932, listed above.

6. Page 313. J. Schultz and T. Dobzhansky (1934), 'The Relation of a Dominant Eye Colour in *Drosophila melanogaster* to the Associated Chromosome Rearrangement', *Genetics*, vol. 19, pp. 344-364.

7. Page 315. On the position effect, see the paper cited in Note 6; also the papers therein referred to.

8. Page 315. On such diverse types in *Datura*, see A. F. Blakeslee (1929), 'Cryptic Types in *Datura*', *Journal of Heredity*, vol. 20, pp. 177-190. For the conditions in *Oenothera*, see R. E. Cleland and A. F. Blakeslee (1931), 'Segmental Interchange, the Basis of Chromosomal Attachments in *Oenothera*', *Cytologia*, vol. 2, pp. 175-233.

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Changes in the Operation of Single Genes. Mutations

Changes in the action of single genes, known as gene mutations, are still more important in bringing about changes in characteristics than are the alterations in grouping of genes and chromosomes described in the preceding chapter. There it was shown that breakage and injury in chromosomes are often accompanied by a change in the action of particular genes situated near the points of breakage, so that chromosome breakage produces gene mutations.

But great numbers of gene mutations were known and studied in detail before it was discovered that such changes may result from breakage or injury to the chromosomes. In such an organism as *Drosophila*, the study of inheritance is based largely on gene mutations; all the recessive characters, and many of the dominant ones, are the result of gene mutations that have occurred since *Drosophila* became an object of experimentation in genetics.¹ Only the so-called 'wild type' or 'normal' characters are not the result of recent mutations. Whether the mutations resulted from breakage or injury to chromosomes is not known; the question is one that is under investigation at the present time.

For a change in inherited characteristics to be identified as a gene mutation, certain conditions must be fulfilled. It must be possible to show that the change is not the result of ordinary recombinations, such as occur in Mendelian inheritance. It must be shown further that it is not a mere result of change of grouping of the genes or chromosomes, such as are described in the preceding chapter. It must be shown that the change in characteristics is due to change in action of a single gene. This is done by a study of the method

of inheritance, by proof that the inheritance is of the 'single factor' or single-gene type, described in previous chapters. These conditions are not easy to fulfil, and recent discoveries, described in the preceding chapter, have much shaken the certainty of the adequacy of such proof. According to one view—the view that some of the so-called mutations are 'position effects', mentioned on page 315—changes that satisfy all tests for gene mutations may result from mere alteration of the relative position of certain genes. On the other hand, the commoner view is that the mutations are essentially alterations in the chemical or physiological constitution of the single genes.

Reserving for later pages the question as to the essential nature of mutations, we examine their occurrence and the genetic phenomena which they present. Mutations occur in organisms subjected to certain conditions, and also in organisms left under natural conditions. We deal first with those occurring under natural conditions.

To ordinary day-by-day observations, mutations appear to occur very infrequently.² Yet when large numbers of individuals are examined for long periods, and the eye is carefully trained for the detection of mutations, the number occurring in even a short period of years is considerable. In the fruit-fly, during twenty-five years of observation, mutations have been seen to occur in several hundred different genes. The gene mutations have occurred in genes that affect all parts and functions of the organism, so that, as before observed, practically all knowledge of heredity in this organism is based on the mutations that have occurred. The ordinary 'wild' individuals are extremely uniform. Mating two of these, the progeny are uniform and there is little opportunity for the study of the rules of inheritance. But when a gene becomes mutated, and the individual carrying it is mated with another in which that gene is not mutated, the descendants display all the rules and proportions of Mendelian heredity. In this way the course of heredity for hundreds of structural and physiological characteristics has been worked out; in each case there has been a mutation in a gene affecting the characteristic.³

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The same single gene, located at a definite point in the genetic system, becomes mutated in different individuals in different ways, so as to give different characteristics in each case. So, in *Drosophila*, there is a gene located at the point 1.5, near one end of the X-chromosome (Fig. 38) which co-operates with other genes in producing the colour of the eye. If this particular gene and the others that work with it are in their usual or 'normal' condition, the colour of the eye is red. If this gene is mutated in a certain way (the other genes remaining unchanged), the eye colour changes to white. Other mutations in this same gene give other eye colours, and in this way, by different mutations of this single gene, a whole series of eye colours has been produced, some eleven or twelve in all. These eye colours, resulting from different mutations, form the series of 'multiple alleles' mentioned on page 176, under the following names: coral, blood, cherry, eosin, apricot, tinged, buff, ecru, ivory, white, ultra-white. Other genes in *Drosophila* and in many other organisms are known thus to have been changed in their effects by mutation in many different ways, so that many series of multiple alleles, or modifications of a single gene, are known to exist.

The change induced by the mutation of a gene may be great, or it may be very small. The eye of the fruit-fly is changed by a certain mutation from red to white, a great change. By another mutation it is changed in a barely detectable way, from red to 'coral'; or 'blood'. Based largely on the so-called mutations of de Vries—which were in fact mainly not gene mutations but the result of chromosomal irregularities—there has been a prevalent tradition that mutations are sudden extensive changes—'saltations', like the change from red eye to white eye. It was natural that the first mutations observed should be these very conspicuous changes: sudden loss of wings or of eyes, or other marked changes in structure. Such conspicuous mutations are indeed not infrequent.

But as studies became more exact and detailed it was found that many mutations produce extremely minute changes, not to be detected without great care. For example, there are known in the fruit-fly a number of gene mutations whose only

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discoverable effect is to cause a very faint lightening of the colour of the eye, in case the individual containing them has eosin-coloured eyes. If the eyes are not eosin-coloured, these mutations have no discoverable effect. The number of gene mutations having such very slight effects is much greater than that of those having marked effects. Most mutations produce barely perceptible changes in characteristics.

The majority of mutations are recessive in heredity. That is, if in one of the pairs of genes one of the two has been mutated, the other not, the mutated gene produces no manifest effect on the individual; the latter remains quite unchanged. Thus one or many gene mutations may have occurred in the chain of genes of a given individual, but so long as only one gene of any pair is affected, there may be no manifest effect. Only when both members of a pair of genes are mutated does the recessive mutation produce its bodily effect. A small proportion of the mutations that occur are dominant; in this case even when but one member of a pair of genes has mutated, the individual is changed by the mutation.

As to the actual time, place and manner of the occurrence of gene mutations, the following may be said. At a given time a mutation occurs in but one of the two genes of any gene pair contained in a cell. Furthermore, it has commonly been held that a mutation occurs at a given time in but a single gene of the long chain of genes (Fig. 36). As shown on page 313, however, this idea requires certain qualifications. It has recently been shown that mutations in several different genes may accompany chromosome breakage. And under radiation several genes of a particular cell may show mutation, possibly due to chromosome breakage of which there is no other evidence. Usually, however, only mutations of single genes have come to the notice of investigators at a given time and in a single cell.

Since most mutations are recessive in their effects, and since only one gene of the pair of genes present is mutated, as a rule the mutation produces no manifest effect on the individual in which it occurs. The fact of its occurrence cannot be detected in that individual. It is only when, by the

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processes of mating in ordinary reproduction, two of the recessive mutations get together in the same pair, in some of the descendants of this individual, that the effect of the mutation appears to view. Thus, when the mutation becomes manifest, it has actually occurred, as a rule, at least two generations earlier, in one of the ancestors of this individual. This relation introduces much difficulty into the study of the time and place at which mutations occur. Many mutations occur that do not come to light for several or many generations; indeed there must exist in any organism many mutations that have never come to light. In the course of generations a large number of recessive mutations may have collected in the chromosomes, none of them producing any effect, because each is accompanied by a normal or unmutated gene of the same pair. If now inbreeding—the mating of close relatives—occurs, a number of these mutated genes may be brought together into the same pairs, in one individual (compare Fig. 61); thereupon the effect of all these mutations suddenly becomes manifested in that individual. Since most mutations are harmful in their effects, this individual will be weak and defective, perhaps in several different ways. This is the reason why inbreeding is harmful; if there were no gene mutations, apparently there would be no disadvantage in the mating of close relatives. One of the chief results of biparental reproduction—what might be called one of its main functions—is that it largely nullifies the effect of harmful mutations.

In view of the fact that mutations may thus remain long hidden, it is fortunate for purposes of study of the occurrence of mutations that in many organisms there is a series of genes, in the X-chromosome of one of the sexes, that are not paired but single. In the best known organisms it is the male that has the single X-chromosome. If in the fertilized egg, or in the cells from which the ovum is derived, a mutation occurs in one of the genes of an X-chromosome, and this passes into a male, the effects of the mutation are at once manifested in the characteristics of that individual. Thus the time and place of the occurrence of gene mutations has been studied most extensively in the genes of the X-chromosome. In recent years,

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however, an elaborate and adequate technique has been devised for bringing to light almost at once the effect of mutations in the genes of any of the chromosomes of *Drosophila*. In this way much has been learned as to the time and place of the occurrence of mutations, and as to the agents causing them.

It has been discovered that a gene mutation may occur in any cell of the body, at any period in the life of the organism. The mutation occurs in but one single cell. If this single cell is the fertilized egg, then all the cells of the body developed from that egg will carry the mutated gene. If the cell in which the mutation occurs is one of the two cells into which the fertilized egg divides, then only half the body will carry that mutation. If the mutation occurs in a cell at a still later stage of development, only a small part of the body will carry the mutated gene. Many cases of such kinds have been thoroughly studied, cases in which one part of the body shows the mutation, the rest not. These are commonly spoken of as somatic mutations. A somatic mutation may affect but few cells. Thus, sometimes through a mutation at a late stage of development, in the gene at locus 1.5 in the X-chromosome of *Drosophila*, a few of the elements of the compound eye may become white, while the remainder of the eye is of the normal red colour.⁴ Such a somatic mutation is not inherited by the offspring of the mutated individual, since the mutation has not changed the genes of the germ cells.

The general upshot of all such studies is to show that gene mutations may occur in any cell of the body, at any period in life. From this it follows that there occur many gene mutations that have no manifested effect whatever; they do not change the characteristics of the individual in which they occur, nor those of his descendants. For example, consider a mutation in a gene that affects the colour of the eye. Eyes derived from the cell in which this mutation occurs will be changed in colour. But many of the cells of the body do not produce eyes; instead they produce legs, wings, parts of the body, or the like. Mutation of an eye-colour gene in such cells will thus have no effect on eye colour, no visible effect on

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any characteristic. It can probably be said with truth that most eye-colour gene mutations have no effect on eye colour, for most of them occur in cells that do not produce eyes. Doubtless there occur great numbers of such mutations that yield no visible effect; any individual may carry many such mutated genes. All such mutations, present in body cells only, are totally lost at the death of the individual carrying them.

What are the agents that produce mutation? For many years after mutations were found to occur, nothing was known as to the agents that cause them. A few genes mutated, as a few of the atoms of a radiant metal disintegrate; in both cases no outside agent appeared to be at work. There seemed to be no relation between the environment and the production of gene mutations. But of late this situation has changed. In 1927, H. J. Muller discovered that by subjecting developing organisms to a powerful dose of X-rays, the genetic system is altered in many ways, and among the rest, the method of action of single known genes is altered: that is, gene mutations are produced.⁵ The X-rays affect other parts of the organisms also. They kill many of them, they leave many others sterile, they cause injuries of many kinds. They cause the chromosomes to break and reunite, in the ways described in the preceding chapter. And they cause numerous gene mutations, which produce in the offspring of the radiated individuals changes in the inherited characteristics, mainly abnormalities, weaknesses and other aberrations from the normal. Such changed characteristics are inherited in later generations by the autosomal or sex-linked methods. The number of visible mutations produced under the action of radiation is about seventy-five times as great as occurs without radiation.

This effect of radiations in producing mutations was confirmed by others and extended to other organisms. Radiations from radium have the same sort of effect as X-rays; they greatly increase the number of gene mutations. Gene mutations have been produced by radiations in maize, barley, tobacco, cotton, various animals, and many other organisms.

By radiation the same types of mutations are produced as occur spontaneously. In many cases the mutations due to the

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radiations are identical with others that had occurred without radiation. Others induced by radiation differ from any before observed. The same gene may be caused by radiation to produce repeatedly in different individuals the same mutation. Since all kinds of mutations are induced by radiation, it is clear that in these cases there is no relation between the kind of mutation produced and the kind of environmental agent that induces them. The mutations induced by radiation are inherited in later generations in the same manner as are those that occur spontaneously.

The number of mutations produced in a given number of individuals is found to increase in proportion to the energy of the radiation; that is, to its intensity and duration, up to an energy that causes injury so great that the radiated germ cells do not develop.

The question arises as to whether the 'spontaneous' mutations are not partly or wholly the result of radiations occurring under natural conditions. It was found that fruit-flies kept in a mining shaft in which natural radiation from the minerals present was abundant gave a larger proportion of mutations than those kept under usual conditions, indicating that the natural radiations are indeed effective in producing mutations. But a very careful study by Muller and Mott-Smith,⁶ based on the fact that the proportional number of mutations varies as the intensity and duration of the radiation, showed that the number of mutations that occur under natural conditions is much greater than can be accounted for by the frequency of natural radiations. It is clear therefore that some other agent is at work.

Another agent has been identified. Muller found that the number of mutations is slightly increased when organisms are kept at a high temperature—29 degrees in place of 20 degrees. Then Goldschmidt, and after him Jollos⁷ employed heat that was destructive, up to 37 degrees. Again, as in the case of radiation, most of the organisms are killed. Again the survivors show injuries and weaknesses of various kinds. And again the progeny of survivors show inherited abnormalities and peculiarities which are found to be due to gene muta-

tions. The same types of mutations are produced by heat as occur spontaneously and under radiation; they are inherited in the same manner.

Certain other matters of great interest have been reported by Goldschmidt and Jollos in connection with the mutations induced by heat. In some of their experimental cultures very great numbers of mutations were produced. It was reported by these authors that the heat produces changes in the bodies of the individuals subjected to the heat, and that in later generations similar inherited changes appear as a result of gene mutations. However, these later mutations did not as a rule appear in the descendants of the particular individuals that had been directly changed by the heat.

In the continuation of this work by Jollos, a further relation, of the very greatest interest, is reported. Subjection of one generation to a high temperature causes a slight inherited effect, due to a slight mutation of a particular gene. Subjection of those changed descendants to the high temperature for another generation is reported to increase the effect and alter the gene still more. By continued subjection to high temperatures for many generations a series of gradations is thus produced, each one hereditary at ordinary temperatures, but passing from slight changes in earlier generations to very great ones in later generations. Thus, in one series of experiments, a certain gene was so altered, in the first generation subjected to heat, as to cause a slight darkening of the body colour. Subjection to heat in later generations increased the effect on this gene until finally the body was black. In another series, the red colour of the eye was, by subjection of successive generations to heat, caused to become lighter and lighter until it was yellowish, and until finally entirely white eyes were produced. The mutations to which these changes in eye colour were due were all in the gene 'white', at the locus 1.5 in the X-chromosome; this is perhaps the best known gene in the fruit-fly. Thus what could be called directed mutations were induced, series of changes in a certain direction for successive generations: what might be called experimental orthogenesis.

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Furthermore, according to Jollos, the nature of the mutations was dependent to some extent on the nature of the conditions under which the organisms were subjected to the heat. Those in moist conditions, for example, gave a different set of mutations from those in dry conditions.

These rather revolutionary conclusions are, however, not confirmed by the extremely extensive and long-continued work of Plough and Ives.⁸ These authors confirm the fact that high temperatures increase the frequency of mutations. But they do not verify the other conclusions of Jollos; and particularly they find no indications of the directed mutations, or orthogenetic series reported by Jollos. As matters stand, the more radical conclusions of Jollos cannot be considered established.

When a mutation has occurred, is the change a permanent one? Or may the genetic system later return to its original condition?

The great majority of mutations appear to be permanent changes. They are inherited by the progeny of the mutated individuals, and such inheritance continues for an indefinite number of generations.

But in recent years a considerable number of cases have been discovered in which the change was not permanent.⁹ Having mutated in a certain way, producing its usual effect on the characteristics, the gene in a later generation returns to its original condition, so that the original characteristics are restored. In some cases such a reversion to normal is produced by subjection of the mutated genes to radiation. In other cases the mutated genes show a marked tendency to revert to the original conditions; reversion occurs in a considerable proportion of them without obvious cause. Sometimes the mutated genes are extremely sensitive to the presence of certain other genes; they revert in their presence but not otherwise. Such behaviour is of much interest in relation to the question as to the essential nature of mutations; some examples will therefore be described.

Demerec¹⁰ found in a species of *Drosophila* (*D. virilis*) that

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a mutation affecting a certain gene at the locus 2.4 in the X-chromosome caused the body to take on a reddish tinge, in place of the normal grey. Another mutation of this same gene caused the body to be yellow in colour. When in the descendants these two differently mutated genes were brought into the same cell (where they form a gene pair, one 'reddish' the other 'yellow'), it was found that in about one-fifth of all the cases in which this was done the genes that had mutated to reddish were transmuted back to the original condition, so that they produced again the original grey colour. This reversion did not occur except in the presence of the yellow gene. Thus the reddish gene is sensitive to the presence of the yellow gene in such a way that it reverts to normal. The reversal occurs only at the time of the reduction division in producing germ cells. The normal genes produced by reversal from the reddish condition remained constantly normal, not later returning to reddish.

As breeding continued for many generations, the proportion of reddish genes that reverted became less. At the end of seven generations reversal had ceased; the reddish gene had become constant. In different families there were different proportions of reversals. By selecting those in which there were fewest reversals, it was possible to obtain families in which the reddish genes were constant, while in other families a part of them underwent reversal.

Thus this mutation exists in two very different conditions: in one it reverts frequently to normal; in the other it is constant. The unstable condition passes into the constant condition.

In the same species of *Drosophila* occurs another inconstant mutation that is of much interest. A certain gene in the X-chromosome was changed by a mutation in such a way as to cause the wings to be small; it is known as miniature. This mutation is in most individuals constant. But in a certain case it was found that this mutation (or another with the same effect) frequently reverts to normal, yielding again large wings. After it has reverted to normal it remains constantly in the normal condition. By selection from different

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families it was possible to obtain some families in which the return of the mutated gene to normal takes place very infrequently. In a group of such families there were but five reversions in 11,609 cases. In other stocks the reversion is frequent, occurring in up to 50 per cent of the cases. The reversion to normal may occur either at the time of the formation of germ cells, or in certain of the body cells. In certain families, however, the reversions occur only in body cells, not in germ cells. In the body cells of males these reversions occur about twice as frequently as in those of females. The frequency of reversal to normal is increased by the presence of certain other mutated genes in the same individuals. It is likewise increased by high temperatures.

Thus again we have a mutation that is constant in some stocks, inconstant and reversible in others. And in some stocks the reversal occurs only in body cells, while in others it occurs in both body cells and germ cells. This mutation is sensitive to the presence of other genes, and to the difference between males and females. Other cases of unstable mutations are known in *Drosophila*.

Extreme cases of unstable mutations, of a different type, are found in certain variegated plants. Here different parts of the plant show different colours of leaves, flowers, fruit or seeds, and it can be shown that these different colours are due to different mutations of certain genes, in the cells that produce the differently coloured parts. This is proved by the fact that when germ cells are produced by the differently coloured parts of the plant, the colour of the parts from which they come is inherited in the offspring produced from the germ cells. This shows that the genes have been altered in the different parts. The inheritance of colour in such cases occurs in the usual Mendelian way, but is usually not complete. That is, in the plants of the next generation there again occur gene mutations, giving rise again to different colours in the different parts of the plant.

Thus, in maize,¹¹ the seed coverings or pericarp on the grains frequently vary in colour, so that on a single ear some of the grains are red, some are white, some are variegated red

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and white, in various degrees. These diversely-coloured seed coverings are part of the parent plant. When from self-fertilized plants, seeds with red pericarp are planted, they produce plants with prevailingly red seeds; seeds with white pericarp yield plants with prevailingly white seeds; seeds with variegated pericarp produce plants that have again variegated seeds. This shows that the genes in the germ cells (seeds) are mutated in the same way as those in the neighbouring body cells (pericarp) of the parent. What has happened is that in early development the genes in certain cells have become mutated in various different ways. From a single such cell are produced later both body cells (pericarp) and germ cells, with the genes so changed as to give a certain colour.

Thus in such cases mutation of some of the genes might be considered a normal feature of the development of the individual. In many animals different parts of the body covering (hair, etc.) are of different colours, as in spotted rabbits, guineapigs and the like. It appears possible that the different colours are due to different mutations of the genes in different parts of the body, such as occur in maize. But in animals there is no way of determining whether this is true, because the different parts of the body do not produce germ cells; the germ cells all come from the germ gland in the interior of the body. This therefore remains an unsettled question.

Are the more common mutations, that appear quite stable, phenomena of a different type from the unstable mutations above described? There are a number of considerations that bear on this question. First, the typical unstable mutations vary in the degree of instability. Second, the same mutation may exist as a stable condition, and in other cases as an unstable one. Third, the unstable mutations may in the course of time pass into the stable condition. Examples of these three types of phenomena we have already seen.

Furthermore, it has been found of late that some of the typical stable mutations may rarely and under special conditions revert to the original normal or wild-type condition. Under the action of X-rays, Patterson and Muller observed in *Drosophila* two reversals of the scute mutation, and seven

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of the forked mutation. Timofeef-Ressovsky made extensive investigations on a number of mutated genes in chromosomes X and III of *Drosophila*.¹² Under radiation he observed 18 reversals to normal out of 289,000 genes radiated. In certain other cases a mutation was transmuted to another condition; thus white eye was transmuted in different cases to eosin, blood, and buff. Johnston and Winchester¹³ radiated 713,000 mutated genes in the X-chromosomes of *Drosophila*; they observed 24 reversions to normal. The particular mutated genes that reverted were: yellow, scute, cut, vermilion, miniature, garnet, forked, and carnation. Reversion of the gene forked occurred 11 times.

Thus it appears that many of the typical constant mutations have not completely lost the capability of returning to the normal wild-type condition, though they do it rarely. The mutational change is not final nor irreversible.

What is the nature of the change in the gene when mutation occurs?

One line of evidence on this question is derived from the relation of the mutated genes to characteristics. On this there are several points that appear of significance:

Injurious Effects of Mutations.—First, there is the fact that when carefully examined most mutations are discovered to be defects. The organism is the worse for their occurrence. These relations are shown in two ways.

On the one hand, the specific effect of the mutations on some particular part or function of the organisms is, in most cases, to bring about a loss or abnormality. Certain mutations cause the body to be distorted, or imperfect in parts, or to lose certain typical structures. Others make the limbs abnormal or small, or result in their total loss. By other mutations the eyes are made imperfect, or very small, or are totally lost. In general, it is true that a part that has been altered by a mutation is not so well adjusted to the rest of the organism or to the surrounding conditions, as it was before the mutation occurred. The general impression from a group of mutated organisms is one of defectiveness and abnormality.

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Further, in addition to their specific effects on particular parts of the body, mutations usually have an injurious effect on the organism as a whole. They weaken the constitution of the individuals in which the mutated genes exist. The result is that the mutated individuals lack resistance to severe conditions, and have a shorter life and a higher mortality rate than those not mutated. Individuals showing the mutated characteristics are difficult to keep alive; specially favourable conditions must be supplied or they perish. Under natural conditions practically all of them die without reproduction, so that the stock is kept free from mutated characteristics.

A large proportion of the mutations that occur cause indeed a complete failure of development, unless the mutated gene is accompanied by a normal gene of the same type. Such lethal mutations occur more frequently than any other type.

Mutations as Partial Inactivation of Genes.—There occur many gene mutations whose effects, both special and general, are so slight that from an examination of the individuals affected by them it is difficult to determine whether they are harmful or not. Even in such cases, however, the gene after mutation has usually a less marked or intense effect than it had before mutation. This is indeed a rather general characteristic of mutated genes; thus, by any mutation of the 'white-eye' gene located at 1.5 in the X-chromosome of *Drosophila*, there is caused a change in eye colour from a deep red to some lighter colour, with less pigment. Such peculiarities have led to the suggestion that the effect of the mutation is partly to inactivate the gene. This suggestion has been confirmed for many mutations by certain results of observation and experiment.¹⁴ These are as follows:

In order that a recessive mutation shall be manifested, it is ordinarily necessary that both the genes of the pair shall be mutated, so that there is no unmutated gene of that type present. But sometimes in one of the two chromosomes of the pair the gene is entirely lost, either by removal of a piece through radiation, or by some other means. Such a chromosome is said to show a deficiency for the gene in question. In such a case therefore but one of the mutated genes is present,

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although there is also no normal dominant gene of that pair present (Fig. 70, B). In such cases, where only one mutated gene is present, it was discovered by Mohr that the effect of the mutation is more pronounced than when two mutated genes are present. This turned out to be the rule for most mutations. Provided no unmutated gene of this pair is present, a single mutated gene produces a greater alteration of the normal character than do two. By the use of radiation it be-

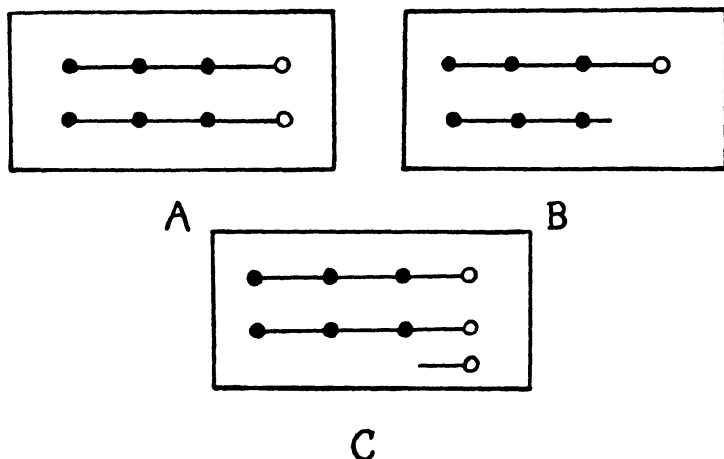


FIG. 70.—Diagram to illustrate the relation of the number of mutated genes (white) to the nature of the characteristic produced. A, Two mutated genes present, the usual condition. B, But one mutated gene present. C, Three mutated genes present. See text.

comes possible to obtain individuals having three examples of a certain mutated gene. This is done as follows: By radiation a small piece of the chromosome containing the mutated gene is broken off, and later, by appropriate breeding, this small piece is introduced into an individual that already has the usual two mutated genes. Thus we obtain an individual containing three of the mutated genes (Fig. 70, C). It is found that such individuals differ less from the normal than those with but two of the mutated genes, and still less than those with but one of the mutated genes. The individuals containing three mutated genes may be almost completely normal.

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The general rule may be expressed as follows: A given mutated gene may be present in either one, two or three 'doses' (Fig. 70). *The greater the number of doses the less the effect of the mutation.*

Certain examples will illustrate these effects. *Cherry* is a recessive mutation of the gene at 1.5 in the X-chromosome of *Drosophila*. The effect of this mutation is to lighten the colour of the eye. When two doses of the mutation are present, the colour is lightened a certain amount. When only one dose is present, the colour is lightened still more. When three doses are present, the colour is hardly lightened at all. This is the usual result with any of the mutational eye colours.

These relations show that what the mutation does is to partly inactivate the gene, so that it no longer produces so great an effect as before. In the case of eye colour, less colour is produced in the mutated gene. But two of the mutated genes produce more colour than one, and three produce still more; almost as much as does the unmutated gene.

This method of action has been demonstrated for many different types of mutation. Thus, the mutation *scute* decreases the number of bristles on the body. If but one *scute* gene is present, the number of bristles is considerably less than normal. If two *scute* genes are present, the number of bristles is greater. If three are present, the number of bristles is almost completely normal.

In some cases it is not at first obvious that the effect of the mutation is a reduction in action as compared with the normal gene, but experiments of the type just described show that this is indeed the case. The body of *Drosophila* carries a large number of simple bristles. By mutation of a certain gene, some of the bristles are caused to be forked instead of simple. But this forked condition is most marked in individuals that have but one of the mutated genes (the other gene of the pair being completely absent). If two of the mutated genes are present, the forking is still perceptible, but is not quite so marked. But if three mutated genes are present, the bristles are much less distinctly forked; they are more like normal simple ones. It appears that the forking is due to the fact that

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certain normal developmental processes are in the mutated individuals not fully carried out; the effect of the mutation is to reduce the normal action. The greater the number of mutated genes present, the more nearly the normal processes are to completion.

Tests of this kind, so far as carried out, indicate that most mutant genes are of this type. The mutational change consists in a reduction of the activity of the normal gene.

In the reversal of mutations, described earlier, in which there is a restoration of the normal condition of the gene, the change is obviously not an inactivation; on the contrary the inactivated gene recovers its activity. Considering such a reactivation as itself a mutation, it is sometimes held that this demonstrates that progressive mutations occur, as well as those that are the reverse of progressive. Recovery of an inactivated gene, however, is obviously a different matter from a progressive change by which a gene would pass into a more active condition that had not before existed.

With the usual nature of gene mutations as inactivations agrees the fact that most mutations are recessive, as compared with the effect of the unmutated gene, so that when the mutated gene and the normal gene are present together, the effect on the characteristics is that of the normal gene alone. The injurious effect of most mutations is likewise in agreement with this. The mutation is a reduction in the activity of the gene, leaving certain developmental processes imperfectly performed.

But in addition to the great majority of gene mutations that are recessive, and result from partial inactivation of the genes, there are less common dominant mutations, which produce an effect even in the presence of the normal gene. Such are in *Drosophila* the mutations abnormal abdomen, bar-eye, notch wings and the like. These have an effect differing from that of the normal gene; they are not mere inactivations. As a rule they produce a disturbance of development, causing it to take an abnormal course. Almost all such dominant genes are lethal when homozygous. It may be remarked that such dominant mutations have of late been shown to be commonly produced by breakage or other injury to chromosomes.

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There are also a few cases of recessive mutations which are not inactivations, but produce an effect differing from that of the normal gene. An example of this is ebony body-colour in *Drosophila*. The mutated gene produces deeper pigmentation than the normal gene.

Though in the overwhelming majority of cases mutations are disadvantageous or can be proved to be partial inactivations of the normal genes, in rare cases mutations have been held to be advantageous. Thus, in the cotton plant there are two varieties, one having forked or deeply cleft leaves, the other leaves that are nearly entire being but slightly lobed. Horlacher and Killough¹⁵ observed that under radiation a mutation from forked leaves to the lobed leaves was produced. As the lobed leaves have more leaf surface, the investigators hold that this mutation may have been beneficial.

Again, in the production of mutations by heat, Jollos found that the red eye of the fruit-fly sometimes mutates to a white colour, without pigment. This is a common mutation, that occurs also under radiation and under natural conditions. It is a typical loss mutation, resulting in a weakening of the constitution, so that under ordinary conditions the mutated flies show a higher mortality than the normal red-eyed individuals. But Jollos finds that the white-eyed flies have a greater resistance to high temperatures than the normal unmutated individuals with red eyes.

Other cases of mutations held to be beneficial could doubtless be found, but they are very rare.

In the preceding chapter it was seen that gene mutations frequently result from breakage of the chromosomes. Certain of the genes at or near the points of breakage change their action, resulting in changes in the inherited characters. Both chromosome breakage and the production of gene mutations occur under radiation. Not all the mutations occurring under radiation are known to be the result of chromosome breakage or other injury, though it is not known that they are not. There are certain other relations between chromosome breakage and the occurrence of mutations that suggest a connection between the two. The number of mutations produced is

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proportional to the energy of the radiation (the intensity multiplied by the time of action), and this also is true for the number of cases of breakage. The actual numbers of mutations produced under radiation is nearly the same as the actual number of cases of breakage. These facts, taken in connection with the known cases in which chromosome breakage induces mutation, suggests that the mutations produced under radiation are indeed the result of chromosome breakage. Certainly this is true for many cases if not for all.

Just what is it in the breakage of chromosomes that brings about the changes known as gene mutations? On the one hand there is the fact of breakage, the tearing apart of structures that were together, with the injuries to tissues that commonly accompany it. The changed action of the genes may be the expression of small-scale injuries, induced at the same time as the greater injuries seen as breaks, deletions and deficiencies. The nature of the changes induced in the genes agrees with this interpretation. The genes are often made unstable. They are as a rule partly inactivated. Their effects on the organism are in almost all cases injurious.

Another change that usually results from the breakage is an alteration in the relation of the genes to each other. When a chromosome breaks, the pieces usually reunite in a changed position, as we have seen, giving inversions or deletions or translocations. The result is that genes near the points of breakage are torn apart from those with which they are normally in close contact, and are brought into close relations with genes other than those that are originally near them. It has been suggested that possibly the effect that a gene produces depends on its position with relation to other genes; that is, presumably on the interaction of genes that are close together. Thus a gene moved to a new position with relation to others produces an effect on development and characteristics that is different from its normal effect, and this changed effect is what has been called a gene mutation. This is spoken of as a 'position effect'. That the 'mutations' which accompany chromosome breakage are such position effects is the view to which a number of recent investigators of these

phenomena have come.¹⁶ If it should turn out to be correct, this would require a reinterpretation of many of the accepted ideas of genetics.

What is certain is that when a gene is brought into a new position as a consequence of the occurrence of a chromosome break close to the point where it is located, it often so changes its action as to give rise to what is called a gene mutation. It is not certain whether this changed action is due to the change of position, or whether it is an expression of injury.

Some questions of great interest remain. Are all gene mutations that occur under the action of radiation the result of chromosome breakage or injury? And further, are all gene mutations of this type? Chromosome breakage, with its further consequences of inversion, translocation, and the like, occurs under natural conditions, as well as under radiation. And the same types of mutations, inherited in the same way, occur under radiation and under natural conditions. It appears possible therefore that all are expressions of such injuries or changes of position.

Relation to Progressive Evolution.—Gene mutations have often been considered as examples of the type of changes that result in progressive evolution. It is obvious that the questions just raised have an important bearing on this conception. If it should turn out that gene mutations are merely 'position effects', changed gene actions resulting from altered relations of genes to each other, they could hardly be considered as steps in progressive evolution. If, on the other hand, it should turn out that gene mutations are expressions of injury to the genes, this also would seem to deprive them of significance as steps in progressive evolution. On the whole, the present state of the evidence seems hardly favourable to the idea that gene mutations of the kinds that have been observed furnish the material for progressive evolution. The overwhelming majority of them are certainly not progressive, not advantageous in their effects. Many cause death, many cause a weakening of the constitution, many cause conspicuous defects and abnormalities. Experiment shows that most of them are reductional in their action, while the few that have

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a positive action different from that of the normal gene are distinctly injurious. Gene mutations are produced by agents (radiation and high temperatures) that are extremely injurious to organisms. And typical gene mutations result from breaks and rearrangements in the genetic system.

While it is thus clear that most gene mutations are not of such a nature as to result in progressive evolution, it is held probable by most students of the matter that among the great number of injurious mutations there may occur a few that are advantageous. It is these that would form the basis for evolutionary progress.

On the other hand, it may turn out that gene mutations of the sort thus far observed are not the material of progressive evolution. It may be that we have not yet recognized the actual steps in progressive evolution, and that when these come clearly into view it will be found that they are not the result of action of destructive agents, or connected with injuries to the genetic system, but rather bear a resemblance to the changes of growth. These questions must be reserved for the future.

NOTES AND REFERENCES ON CHAPTER 14

1. Page 319. Many of the references given at the end of Chapter 13 deal with mutations as well as with other genetic variations. See particularly those cited in Notes 1 and 4 of Chapter 13.

2. Page 320. On the frequency of mutations, see H. J. Muller (1928), 'The Measurement of Gene Mutation Rate in *Drosophila*, Its High Variability and Its Dependence on Temperature', *Genetics*, vol. 13, pp. 279-357.

3. Page 320. On the characteristics resulting from mutation in *Drosophila*, see Note 1 to Chapter 1.

4. Page 324. On somatic mutations in *Drosophila*, see J. T. Patterson (1929), 'The Production of Mutations in Somatic Cells of *Drosophila melanogaster* by Means of X-rays', *Journal of Experimental Zoology*, vol. 53, pp. 327-372.

5. Page 325. H. J. Muller (1927), 'Artificial Transmutation of the Gene', *Science*, vol. 66, pp. 84-87. See also the papers by Muller listed in Note 4, Chapter 13.

6. Page 326. H. J. Muller and L. M. Mott-Smith (1930), 'Evidence that Natural Radioactivity is Inadequate to Explain

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the Frequency of "Natural" Mutations', *Proc. of the National Academy of Sciences*, vol. 16, pp. 277-285.

7. Page 326. R. B. Goldschmidt (1929), 'Experimentelle Mutation und das Problem der sogenannten Parallelinduktion. Versuche an *Drosophila*', *Biologisches Zentralblatt*, Bd. 49, pp. 437-448. —V. Jollos (1930), 'Studien zum Evolutionsproblem, I. Über die experimentelle Hervorrufung und Steigerung von Mutationen bei *Drosophila melanogaster*', *Biologisches Zentralblatt*, Bd. 50, pp. 541-554.

8. Page 328. H. H. Plough and P. T. Ives (1935), 'Induction of Mutations by High Temperature in *Drosophila*', *Genetics*, vol. 20, pp. 42-69.

9. Page 328. On unstable mutations, see H. Stubbe (1933), 'Labile Gene', *Bibliographia Genetica*, vol. 10, pp. 299-356.

10. Page 328. M. Demerec (1926), 'Reddish—A Frequently "Mutating" Character in *Drosophila virilis*', *Proc. Nat. Acad. Sci.*, vol. 12, pp. 11-16. —(1926), 'Miniature-Alpha—A Second Frequently Mutating Gene in *Drosophila virilis*', *Proc. Nat. Acad. Sci.*, vol. 12, pp. 687-690.

11. Page 330. For an account of variegation in maize, see W. H. Eyster (1924), 'A Genetic Analysis of Variegation', *Genetics*, vol. 9, pp. 372-404.

12. Page 332. Reviewed in the paper of Stubbe, Note 9 above.

13. Page 332. O. Johnston and A. M. Winchester (1934), 'Reverse Mutations in *Drosophila melanogaster*', *Amer. Naturalist*, vol. 68, pp. 351-358.

14. Page 333. See the account in the paper of H. J. Muller (1932), referred to in Note 4, Chapter 13.

15. Page 337. W. R. Horlacher and D. T. Killough (1933), 'Progressive Mutations Induced in *Gossypium hirsutum* by Radiations', *Amer. Naturalist*, vol. 67, pp. 532-538.

16. Page 339. For discussion of the 'position effect', see the paper of Schultz and Dobzhansky, referred to in Note 6 of Chapter 13, and the other papers referred to by these two authors.

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